

Incubation periods

Questions may either ask directly about incubation periods or they may be used to provide a clue in a differential diagnosis

Less than 1 week

- meningococcus
- diphtheria
- influenza
- scarlet fever

1 - 2 weeks

- malaria
- typhoid
- dengue fever
- measles

2 - 3 weeks فيروسات العيال

- mumps
- rubella
- chickenpox

Longer than 3 weeks الفيروسات الشهيبة

- infectious mononucleosis EBV
- cytomegalovirus CMV
- viral hepatitis
- HIV

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Congenital infections

- The major congenital infections in examinations are rubella, toxoplasmosis and CMV
- Cytomegalovirus is the most common congenital infection in the UK.
- Maternal infection is usually asymptomatic

	Rubella الحصبة الألمانية	Toxoplasmosis	Cytomegalovirus
Characteristic features	1) Sensorineural deafness 2) Congenital cataracts 3) Glaucoma 4) Congenital heart disease (e.g. PDA)	1) Cerebral calcification 2) Chorioretinitis 3) Hydrocephalus	1) Growth retardation 2) Purpuric skin lesions, (Pinpoint petechial blue-berry muffin)
Other features	1) Growth retardation 2) Hepatosplenomegaly 3) Purpuric skin lesions 'Salt and pepper' 4) Chorioretinitis 5) Microphthalmia 6) Cerebral palsy	1) Anaemia 2) Hepatosplenomegaly 3) Cerebral palsy	1) Sensorineural deafness 2) Encephalitis/seizures 3) Cerebral palsy 4) Pneumonitis 5) Hepatosplenomegaly 6) Anaemia 7) Jaundice

التلاثة يعملوا Cerebral palsy, Hepatosplenomegaly

Bacterial Infections

Classification of bacteria

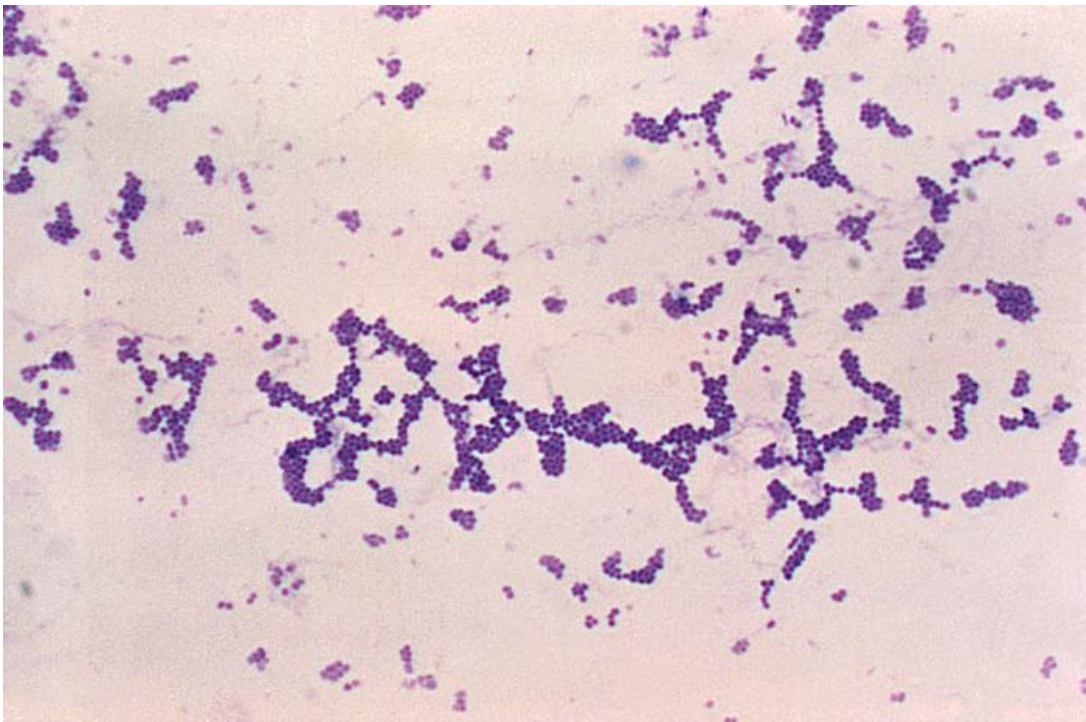
Remember:

- **Gram positive cocci** = staphylococci + streptococci (including enterococci)
- **Gram negative cocci** = *Neisseria meningitidis* + *Neisseria gonorrhea*, also *Moraxella*

Therefore, only a small list of **Gram positive rods** (bacilli) need to be memorized to categorize all bacteria - mnemonic = ABCD L

- Actinomyces
- *Bacillus anthracis* (anthrax)
- Clostridium
- Diphtheria: *Corynebacterium diphtheriae*
- *Listeria monocytogenes*

—→ Remaining organisms are **Gram negative rods**



The Gram stain shows Gram positive cocci growing in clusters, typical of *Staphylococcus aureus*.

This is the most likely organism to cause post-operative infection of prosthetic joints within the first one to four weeks following surgery.

Staphylococci

- Staphylococci are a common type of bacteria which are often found normal commensal organisms but may also cause invasive disease.
- **Some basic facts include:**
 - 1) Gram-positive cocci
 - 2) facultative anaerobes
 - 3) produce catalase

The two main types are *Staphylococcus aureus* and *Staphylococcus epidermidis*.

Staphylococcus aureus	Staphylococcus epidermidis
• Coagulase-positive • Causes: ⇒ skin infections (e.g. cellulitis), ⇒ abscesses, ⇒ osteomyelitis, ⇒ toxic shock syndrome	• Coagulase-negative • Causes: ⇒ central line infections and ⇒ infective endocarditis, ⇒ peritonitis in PD patients

- *Staphylococcus aureus* is Gram positive, in **irregular clusters**, produces catalase and coagulase.
- *Staphylococcus albus* is Gram positive, producing catalase but does not produce coagulase.
- *Streptococcus pyogenes* is Gram positive in chains and does not produce catalase.
- *H. influenzae* is Gram negative bacilli.
- *Pseudomonas aeruginosa* is Gram negative bacilli.

Osteomyelitis

- Osteomyelitis describes an infection of the bone.
- **Staph. aureus** is the most common cause except in patients with sickle-cell anaemia where **Salmonella** species predominate.

Predisposing conditions:

- 1) diabetes mellitus
- 2) sickle cell anaemia
- 3) intravenous drug user
- 4) immunosuppression due to either medication or HIV
- 5) alcohol excess

Investigations:

- MRI is the imaging modality of choice, with a sensitivity of 90-100%

Management:

- flucloxacillin for 6 weeks
- clindamycin if penicillin-allergic

Gonococcal infection being the most common cause of septic arthritis in **young adults**

Staphylococcal toxic shock syndrome

- Staphylococcal toxic shock syndrome describes a severe systemic reaction to staphylococcal exotoxins. (toxic shock syndrome toxins TSS-1, TSS-2)
- It came to prominence in the early 1980's following a series of cases related to infected tampons
- Although the earliest described cases involved mostly menstruating women using highly absorbent tampons, only 55% of current cases are associated with menstruation.
- The illness can also occur in children, postmenopausal women, and men.

Risk factors include:

- Recent menstruation
- Recent use of barrier contraceptives such as diaphragms and vaginal sponges
- Vaginal tampon use (especially prolonged)
- Recent childbirth
- Recent surgery, and
- Current *S. aureus* infection.

Centers for Disease Control and Prevention diagnostic criteria

- 1) fever: temperature $> 38.9^{\circ}\text{C}$
- 2) hypotension: systolic blood pressure < 90 mmHg
- 3) diffuse erythematous rash
- 4) **desquamation of rash**, especially of the **palms** and **soles**
- 5) Involvement of 3 or more organ systems: e.g.
 - ⇒ GIT (diarrhoea and vomiting),
 - ⇒ mucous membrane erythema,
 - ⇒ renal failure,
 - ⇒ hepatitis,
 - ⇒ thrombocytopenia,
 - ⇒ CNS (e.g. confusion)

Blood cultures may be positive for *S. aureus*.



MRSA

- Methicillin-resistant Staphylococcus aureus (MRSA) was one of the first organisms which highlighted the dangers of hospital-acquired infections.
- Who should be screened for MRSA?
 - 1) All patients awaiting elective admissions
Exceptions include:
 - ⇒ day patients having terminations of pregnancy and ophthalmic surgery
 - ⇒ Patients admitted to mental health trusts are also excluded
 - 2) from 2011 all emergency admissions will be screened
- How should a patient be screened for MRSA?
 - 1) nasal swab and skin lesions or wounds
 - 2) the swab should be wiped around the inside rim of a patient's nose for 5 seconds
 - 3) the microbiology form must be labelled 'MRSA screen'
- Suppression of MRSA from a carrier once identified:
 - 1) nose: mupirocin 2% in white soft paraffin, tds for 5 days
 - 2) Skin:
 - ⇒ chlorhexidine gluconate, od for 5 days
 - ⇒ Apply all over but particularly to the axilla, groin and perineum
- The following antibiotics are commonly used in the treatment of MRSA infections:
 - 1) vancomycin
 - 2) teicoplanin
 - 3) linezolid
- Some strains may be sensitive to the antibiotics listed below but they should not generally be used alone because resistance may develop:
 - 1) rifampicin
 - 2) macrolides
 - 3) tetracyclines
 - 4) aminoglycosides
 - 5) clindamycin
- Relatively new antibiotics have activity against MRSA but should be reserved for resistant cases such as:
 - 1) linezolid,
 - 2) quinupristin/dalfopristin combinations
 - 3) tigecycline

The most effective single step to reduce incidence of MRSA is **hand hygiene**

What is the basis of methicillin resistance in Staphylococci?

- Modification of target penicillin-binding proteins
- The resistant organisms produce PBPs that have a low affinity for binding beta-lactamase antibiotics. Other organisms which do the same are Pneumococci and Enterococci.

Teicoplanin (Targocid):

- Used in prophylaxis and treatment of serious infections by Gram+ve bacteria, including MRSA & Enterococcus faecalis
- It is a semisynthetic glycopeptide with a spectrum similar to vancomycin.
- It inhibits bacterial cell wall synthesis.

Tigecycline (Tygacil):

- Was developed in response to growing prevalence of Ab. resistance in bacteria as Staph. aureus and Acinetobacter baumannii.
- Tygacil is the first clinically available drug in a new class called glycylcyclines.
- It is structurally similar to tetracyclines (contains a central 4-ring carbocyclic skeleton and is a derivative of minocycline).
- Tigecycline is bacteriostatic
- Inhibit protein synthesis by binding to the 30S ribosomal subunit

Anaerobic activity

The following antibiotics have anti-anaerobic activity

- 1) Penicillins
- 2) Cephalosporins (except ceftazidime)
- 3) Erythromycin
- 4) Metronidazole
- 5) Tetracycline

The following antibiotics do not have anti-anaerobic activity GCC

- 1) Gentamicin
- 2) Ciprofloxacin
- 3) Ceftazidime

Linezolid

- Linezolid is a type of oxazolidonone antibiotic which has been introduced in recent years.
- It inhibits bacterial protein synthesis by stopping formation of the 70s initiation complex
- It is **bacteriostatic** nature.

Spectrum: highly active against Gram positive organisms including:

- 1) MRSA (Methicillin-resistant Staphylococcus aureus)
- 2) VRE (Vancomycin-resistant enterococcus)
- 3) GISA (Glycopeptide Intermediate Staphylococcus aureus)

Adverse effects:

- **thrombocytopenia** (reversible on stopping)
- **MAOI** monoamine oxidase inhibitor: avoid tyramine containing foods (Cheese reaction)

Trimethoprim

Trimethoprim is an antibiotic, mainly used in the management of urinary tract infections.

Mechanism of action

- interferes with DNA synthesis by inhibiting dihydrofolate reductase

Adverse effects

- myelosuppression
- transient rise in creatinine: trimethoprim competitively inhibits the tubular secretion of creatinine resulting in a temporary increase which reverses upon stopping the drug

Streptococci

- Streptococci are gram-positive cocci.
- They may be divided into alpha and beta hemolytic:

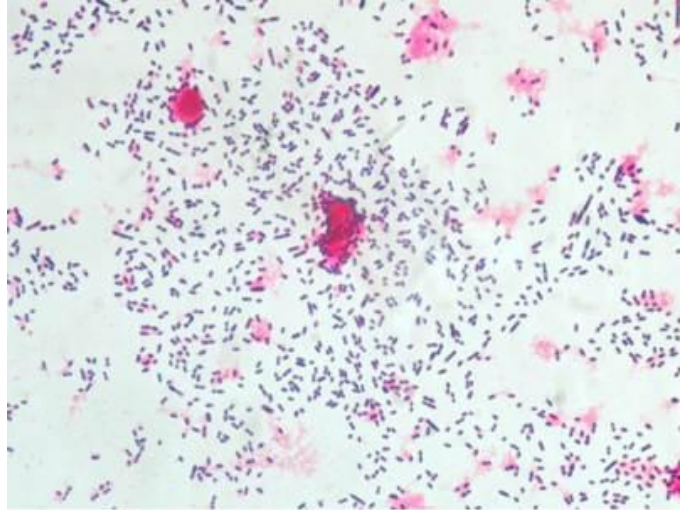
Alpha haemolytic streptococci (partial haemolysis)

- The most important alpha haemolytic Streptococcus is *Streptococcus pneumonia* (*pneumococcus*) and *Streptococcus viridans*

Pneumococcus

is a common cause of:

- 1) pneumonia,
- 2) meningitis and
- 3) otitis media



The Gram stains shows Gram positive diplococci, characteristic of *Streptococcus pneumoniae*.

Beta haemolytic streptococci (complete haemolysis)

- These can be subdivided into groups A-H.
- Only groups A, B & D are important in humans.

Group A

- most important organism is *Streptococcus pyogenes*
- responsible for:
 - 1) erysipelas,
 - 2) impetigo,
 - 3) cellulitis,
 - 4) type 2 necrotizing fasciitis and
 - 5) pharyngitis/tonsillitis
- 6) immunological reactions can cause:
 - ⇒ rheumatic fever or
 - ⇒ post-streptococcal glomerulonephritis
 - ⇒ Henoch-Schönlein purpura (HSP)
- 7) erythrogenic toxins cause scarlet fever

Group B

- *Streptococcus agalactiae* may lead to:
 - ⇒ neonatal meningitis and
 - ⇒ septicaemia

Group D

- *Enterococcus*

Necrotising fasciitis

- Necrotising fasciitis is a medical emergency that is difficult to recognise in the early stages
- It can be classified according to the causative organism:
 - type 1 is caused by mixed anaerobes and aerobes (often post-surgery in diabetics)
 - type 2 is caused by *Streptococcus pyogenes*

Features:

- **acute onset**
- **painful**, erythematous lesion develops
- **extremely tender** over infected tissue

Management:

- 1) urgent surgical referral for debridement هام جدا
 - 2) intravenous antibiotics **Clindamycin & benzylpenicillin**
- ☒ Clindamycin is used as it not only destroys the bacteria but also neutralises the toxin released by the bacteria.
 - ☒ Group A *Streptococci* are usually very sensitive to benzylpenicillin so this is frequently added though this does not neutralise the toxin.

Gram Negative Cocci

- Neisseria meningitidis
- Neisseria gonorrhea
- Moraxella

Neisseria meningitidis

Presentation of meningococcal disease:

- 15% - meningitis
- 25% - septicaemia
- 60% - a combination of meningitis and septicaemia

Meningococcal septicaemia

- Meningococcal septicaemia is a frightening condition for patients, parents and doctors.
- It is associated with a high morbidity and mortality unless treated early.
- Meningococcal disease is the leading infectious cause of death in early childhood.
- A high index of suspicion is therefore needed.
- Much of the following is based on the 2010 NICE guidelines

Investigations:

- 1) blood cultures
- 2) blood PCR
- 3) ~~lumbar puncture~~ is usually **contraindicated**
- 4) full blood count and clotting to assess for DIC



The picture shows a purpuric rash of meningococcal septicaemia

Meningitis

Causes

0 - 3 months

- Group B Streptococcus (*Streptococcus agalactiae*) (most common cause in neonates)
- *E. coli*
- *Listeria monocytogenes*

3 months - 6 years

- *Neisseria meningitidis*
- *Streptococcus pneumoniae* (Alpha haemolytic streptococci)
- *Haemophilus influenzae*

6 years - 60 years

- *Neisseria meningitidis*
- *Streptococcus pneumoniae* (Alpha haemolytic streptococci)

> 60 years

- *Streptococcus pneumoniae* (Alpha haemolytic streptococci)
- *Neisseria meningitidis*
- *Listeria monocytogenes*

Immunosuppressed

- *Listeria monocytogenes*

Investigations suggested by NICE

- 1) full blood count
- 2) CRP
- 3) coagulation screen
- 4) blood culture
- 5) whole-blood PCR
- 6) blood glucose
- 7) blood gas

Lumbar puncture if no signs of raised intracranial pressure

Listeria meningitis

- ☒ Should always be considered in patients with meningitis associated with **brain stem involvement (ataxia)**, and in immunosuppressed patients.
- ☒ The treatment of choice is **gentamicin and ampicillin**.
- ☒ Neutrophils usually predominate in the cerebrospinal fluid (CSF) in patients with bacterial meningitis. However, a lymphocytosis is seen in approximately 10% of patients.
- ☒ Lymphocytes may predominate in 30% of patients with meningitis caused by Gram negative bacilli, or in *Listeria monocytogenes* infection.
- ☒ Note that this means that 70% of patients with *Listeria meningitis* will have a neutrophilic CSF.
- ☒ A lymphocytic CSF predominates in TB and fungal meningitis.

Meningitis management

- All patients should be transferred to hospital urgently.
- If patients are in a pre-hospital setting (for example a GP surgery) and meningococcal disease is suspected then **intramuscular benzylpenicillin** may be given, as long as this doesn't delay transit to hospital.

BNF recommendations on antibiotics

Scenario	BNF recommendation
Initial empirical therapy aged 3 months-50yr	Intravenous cefotaxime
Pneumococcal meningitis or Haemophilus influenza.	
Initial empirical therapy aged < 3 months	Intravenous cefotaxime + amoxicillin
Initial empirical therapy aged > 50 years	
Meningococcal meningitis	Intravenous benzylpenicillin or cefotaxime
Meningitis caused by Listeria	Intravenous amoxicillin + gentamicin

If the patient has a history of immediate hypersensitivity reaction to penicillin or to cephalosporins the BNF recommends using **chloramphenicol**

Management of contacts:

A) Meningococcal meningitis

- ☒ the risk is highest in the first 7 days but **persists for at least 4 weeks**

1) Antibiotic prophylaxis

- ⇒ needs to be offered to household and close contacts of affected patients
- ⇒ **Oral ciprofloxacin** or **rifampicin** or may be used.
- ⇒ The Health Protection Agency (HPA) guidelines now state that whilst either may be used **ciprofloxacin is the drug of choice** as it is widely available and only requires one dose

2) meningococcal vaccination

- ⇒ should be offered to close contacts when serotype results are available
- ⇒ booster doses to those who had the vaccine in infancy

B) Pneumococcal meningitis

1) No prophylaxis is generally needed.

2) There are however exceptions to this:

- ⇒ If a cluster of cases of pneumococcal meningitis occur the HPA have a protocol for offering close contacts **antibiotic prophylaxis**.

Gram Negative Cocci

- Neisseria meningitidis
- Neisseria gonorrhea
- Moraxella

Neisseria gonorrhea

Gonorrhea

- Caused by the Gram negative intracellular diplococcus Neisseria gonorrhea.
- Acute infection can occur on any mucous membrane surface, typically genitourinary but also rectum and pharynx.
- The incubation period of gonorrhea is 2-5 days

Features:

- 1) males: urethral discharge, dysuria
- 2) females: cervicitis leading to vaginal discharge
- 3) rectal and pharyngeal infection is usually asymptomatic
- 4) Local complications that may develop include urethral strictures, epididymitis and salpingitis (hence may lead to infertility).
- 5) Disseminated infection may occur - see below

Management: **Ceftriaxone + azithromycin**

- 1) The 2011 British Society for Sexual Health and HIV (BASHH) guidelines recommend:
 - ⇒ **Ceftriaxone 500 mg intramuscular** as a **single dose** with **azithromycin 1 g oral** as a **single dose**.
 - ⇒ The azithromycin is thought to act synergistically with ceftriaxone and is also useful for **eradicating any co-existent Chlamydia infections**
- 2) if ceftriaxone is refused or contraindicated other options include **cefixime 400mg PO** (**single dose**)

☒ Ciprofloxacin:

- ⇒ Used to be the treatment of choice.
- ⇒ However, **there is increased resistance to ciprofloxacin** and therefore **cephalosporins** are now used

Disseminated gonococcal infection (DGI) **and gonococcal arthritis**

- Gonococcal infection being the most common cause of septic arthritis in **young adults**.
- The pathophysiology of DGI is not fully understood
- It is thought to be due to haematogenous spread from mucosal infection (e.g. asymptomatic genital infection).

Initially:

There may be a **classic triad**: (**Key features of disseminated gonococcal infection**)

- 1) Tenosynovitis
- 2) migratory polyarthritis
- 3) dermatitis (lesions can be maculopapular or vesicular)

Later complications include

⇒ septic arthritis, endocarditis and perihepatitis (Fitz-Hugh-Curtis syndrome)

Treatment: IV broad spectrum **cephalosporins** (ceftriaxone 1 g od) for 7 days.

Gram positive bacillus

Gram positive rods (bacilli) mnemonic = ABCD L

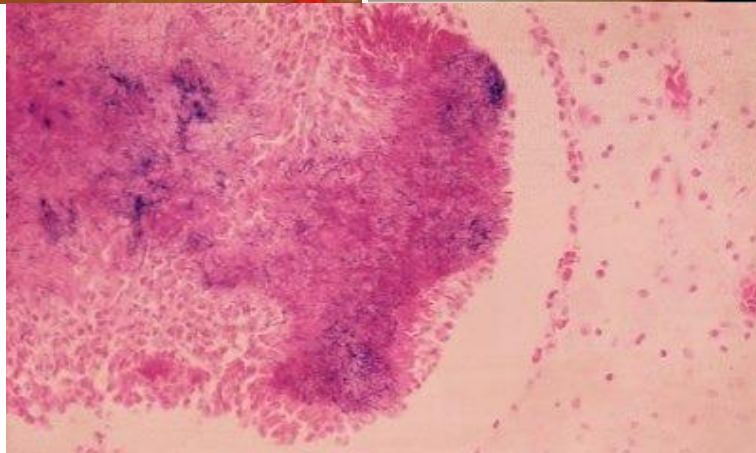
- Actinomyces
- Bacillus anthracis (anthrax)
- Clostridium
- Diphtheria: Corynebacterium diphtheriae
- Listeria monocytogenes

Actinomyces

- Caused by a filamentous, Gram positive bacterium.
 - The commonest agent is Actinomyces israelii.
 - Several clinical syndromes are observed
- 1) **Cervicofacial actinomyces**,
 - ☒ In which there is a soft tissue swelling often discharging yellow granular material ('sulphur granules') via a sinus.
 - 2) **Abdominal and pelvic actinomyces**
 - ☒ Usually follows introduction of the organism through surgery (for example, laparotomy, perforation, cholecystitis) or
 - ☒ From intrauterine device placement.
 - 3) **Thoracic actinomyces**,
 - ☒ Affecting lungs, pleura and/or mediastinum
 - ☒ Follows aspiration or spread from the neck or abdomen.
 - 4) **Central nervous system actinomyces**
 - ☒ Occurs following haematogenous spread of the organism
 - ☒ usually presents as a single multi-loculated cerebral abscess

Treatment:

- ☒ High dose intravenous **benzyl penicillin** and **surgical resection/drainage**.



Gram positive bacillus

Bacillus anthracis

Anthrax

- Anthrax is caused by **Bacillus anthracis**, a Gram positive rod.
- It is spread by infected carcasses. جثث
- It is also known as Woolsorters' disease. فارزي الصوف
- **Bacillus anthracis produces a tripartite protein toxin**
 - 1) protective antigen
 - 2) oedema factor: a bacterial adenylate cyclase which increases cAMP
 - 3) lethal factor: toxic to macrophages



Features:

- 1) Following animal or animal product exposure:
 - ⇒ The skin lesion evolves over ~**2 weeks** into a papule, pustule, vesicle and eventually forms an ulcer with a central black eschar (painless). (cutaneous malignant pustule , but no pus)
- 2) The ulcer typically **painless** and **non-tender**
- 3) The surrounding skin is usually boggy and **oedematous**
- 4) **tender regional LNs**
- 5) anthrax can cause **gastrointestinal bleeding**

Management:

- 1) the current Health Protection Agency advice for the initial management of cutaneous anthrax is **ciprofloxacin**
- 2) further treatment is based on microbiological investigations and expert advice
- 3) Lesions heal spontaneously in 80-90% of cases;
- 4) **10-20%** of patients progress and become bacteraemic -with a high mortality. **Penicillin** is effective in treating the infection.

Gram positive bacillus

Listeria

Low temperatures

- Listeria monocytogenes is a **Gram positive bacillus**
- has the unusual ability to multiply at low temperatures
- It is typically spread via contaminated food, typically unpasteurized dairy products.
- Infection is particularly dangerous to the unborn child where it can lead to **miscarriage**

Features - can present in a variety of ways

- 1) diarrhoea, flu-like illness
- 2) pneumonia , **meningoencephalitis**
- 3) **ataxia** and seizures

Investigation:

- 1) Suspected Listeria infection should be investigated by taking **blood cultures**.
- 2) **CSF** may reveal a **pleocytosis**, with '**tumbling motility**' on wet mounts

Management:

- 1) Listeria is sensitive to **amoxicillin/ ampicillin** (cephalosporins usually inadequate)
- 2) **Listeria meningitis** should be treated with **IV amoxicillin/ampicillin + gentamicin**

تتكاثر في البرد وبتيجى من اللبن وتعمل اى اعراض وتعمل مزرعة دم
تلاقى حركة زاحفة على جبال رطبة.....
وتتعالج بالبنسلين مش بالكيفالوسبورين.....
كثرة خلايا السائل النخاعي = pleocytosis

Gram positive bacillus

Diphtheria

Caused by the Gram positive (rods) bacterium *Corynebacterium diphtheriae*

Pathophysiology:

- releases an **exotoxin** encoded by a **β -prophage**
- exotoxin **inhibits protein synthesis** by catalyzing **ADP-ribosylation** of **elongation factor EF-2**
- Diphtheria toxin commonly causes a **diphtheric membrane** on tonsils caused by necrotic mucosal cells.
- Systemic distribution may produce necrosis of myocardial, neural and renal tissue

Possible presentations:

- 1) recent visitors to Eastern Europe/Russia/Asia, Fever.....راجع من روسيا او اوربا الشرقية
- 2) sore throat with a diphtheric membrane
- 3) bulky cervical lymphadenopathy
- 4) neuritis e.g. cranial nerves, peripheral neuropathy
- 5) heart block

Treatment consists of antibiotic therapy (penicillin) and diphtheria antitoxin.



Gram Positive Bacillus

Tuberculosis

Diagnosis:

- Small **aerobic non-motile bacillus**.
- It is classified as a **Gram positive** but **stains very weakly** on testing.
- When using the Ziehl-Neelsen test it stains **bright red** against a **blue background**.
 - 1) In adults induction of sputum or bronchoscopy and lavage may be used in patients who cannot produce sputum
 - 2) In children who are unable to cough up sputum, the gold standard is gastric washings for M tuberculosis culture

Tuberculosis drug therapy:

1) The standard therapy for treating active tuberculosis:

A) Initial phase - first 2 months (RIPE)

- 1) Rifampicin
- 2) Isoniazid
- 3) Pyrazinamide
- 4) Ethambutol
(the 2006 NICE guidelines now recommend giving a 'fourth drug' such as ethambutol routinely - previously this was only added if drug-resistant tuberculosis was suspected)

B) Continuation phase - next 4 months

- 1) Rifampicin
- 2) Isoniazid

2) The treatment for latent tuberculosis:

- ☒ Patients with infection but no evidence of disease (strong positive mantoux), should receive prophylaxis with:
 - ⇒ **isoniazid alone for 6 months (+ pyridoxin)** or
 - ⇒ **isoniazid and rifampicin for 3 months.**

3) Patients with meningeal tuberculosis:

- ☒ treated for a prolonged period (at least **12 months**)
- ☒ with the addition of **steroids**

4) Directly observed therapy:

- ☒ a **three times a week dosing** regimen
- ☒ May be indicated in certain groups, including:
 - 1) homeless people with active tuberculosis
 - 2) patients who are likely to have poor concordance
 - 3) all prisoners with active or latent tuberculosis

- ☒ The metabolism of corticosteroids is increased by rifampicin.
- ☒ Patients on long term steroids should have their dose of steroids increased when starting antituberculous therapy.

Drug side-effects and mechanism of action

Rifampicin

- 1) **mechanism of action: inhibits** bacterial DNA dependent **RNA polymerase** preventing transcription of DNA into mRNA
- 2) potent liver enzyme inducer
- 3) hepatitis, orange secretions
- 4) flu-like symptoms

Isoniazid

- 1) **mechanism of action: inhibits** mycolic acid synthesis
- 2) **peripheral neuropathy**: prevent with pyridoxine (Vitamin B6)
- 3) hepatitis, agranulocytosis, **SLE**
- 4) liver enzyme inhibitor
- 5) **Isoniazid toxicity** should be suspected in any patient with:
 - ⇒ Intractable seizures and
 - ⇒ Profound metabolic acidosis with high AG.
 - ☒ **Intravenous pyridoxine** (vitamin B6) is the treatment of choice.

Pyrazinamide

- 1) **mechanism of action**: converted by pyrazinamidase into pyrazinoic acid which in turn **inhibits fatty acid synthase** (FAS) I
- 2) hyperuricaemia causing **gout**
- 3) arthralgia, myalgia, **SLE**
- 4) hepatitis

Ethambutol

- 1) **mechanism of action**: inhibits the enzyme **arabinosyl transferase** which polymerizes arabinose into arabinan
- 2) **optic neuritis**: check visual acuity before and during treatment
- 3) dose needs adjusting in patients with **renal impairment**

- Ethambutol may produce optic neuritis which appears to be related to dose and duration of treatment.
- Symptoms generally start between 4 months and 1 year after starting therapy.
- The effects are generally reversible.
- In rare cases recovery may be delayed for one year or more and the effect may possibly be irreversible in these cases.

Tuberculosis screening

- The Mantoux test is the main technique used to screen for latent tuberculosis.
- **The T-SPOT.TB test** (interferon-gamma blood test) is a revolutionary in vitro diagnostic assay that measures T cells primed to Mycobacterium tuberculosis (MTB) antigens.
- It is used in a number of specific situations such as:
 - the Mantoux test is positive or equivocal
 - people where a tuberculin test may be falsely negative (see below)

Mantoux test

- 0.1 ml of 1:1,000 purified protein derivative (PPD) injected intradermally
- result read 2-3 days later

Diameter of induration	Positivity	Interpretation
< 6mm	• Negative • no significant hypersensitivity to tuberculin protein	⇒ Previously unvaccinated individuals ⇒ may be given the BCG
6 - 15mm	• Positive • hypersensitive to tuberculin protein	⇒ Should not be given BCG. ⇒ May be due to previous TB infection or BCG
> 15mm	• Strongly positive • strongly hypersensitive to tuberculin protein	⇒ Suggests tuberculosis infection .

False negative tests may be caused by:

- 1) miliary TB
- 2) sarcoidosis
- 3) HIV
- 4) lymphoma
- 5) very young age (e.g. < 6 months)

Heaf test

- The Heaf test was previously used in the UK but has been since been discontinued. It involved injection of PPD equivalent to 100,000 units per ml to the skin over the flexor surface of the left forearm. It was then read 3-10 days later.

This patient has a **fish-tank granuloma**, caused by the atypical mycobacterium, *Mycobacterium marinum*.

It is found in ornamental fish أسماك الزينة and is commonly seen in individuals who rear fish as a hobby.



Gram positive bacillus

Clostridium

Clostridium perfringens

- ⇒ Produces α -toxin, a lecithinase,
- ⇒ Causes gas gangrene (myonecrosis) and haemolysis.

Clostridium tetani neurotoxin

- ⇒ Tetanospasmin which blocks the release of GABA and glycine.
- ⇒ Causes Lockjaw

Clostridium botulinum

- ⇒ produces an exotoxin that blocks acetylcholine (ACh) release
- ⇒ leading to flaccid paralysis

Gas gangrene

- Caused by *Clostridium perfringens* (or other *Clostridium* spp).
- Infection follows trauma and contamination of the wound by soil containing clostridial spores.
- Patients with gas gangrene tend to be more systemically unwell than the degree of cellulitis would suggest and urgent surgical attention may prevent death.
- The diagnosis is often a clinical one; however, it may be confirmed on culture of wound samples.
- Pt needs aggressive surgical debridement, high dose benzyl-penicillin and clindamycin, and hyperbaric oxygen if available.

Tetanus

- Caused by tetanospasmin exotoxin released from *Clostridium tetani* (gram positive rods).
- Tetanus spores are present in soil and may be introduced into the body from a wound, which is often unnoticed.
- Tetanospasmin blocks the release of GABA and glycine.

Features:

- 1) prodrome fever, lethargy, headache
- 2) trismus (lockjaw)
- 3) risus sardonicus, opisthotonus (arched back, hyperextended neck)
- 4) spasms (e.g. dysphagia)

Management:

- 1) supportive therapy including **ventilatory support** and **muscle relaxants**
- 2) **intramuscular human tetanus immunoglobulin** for high-risk wounds
(Compound fractures, delayed surgical intervention, significant degree of devitalised tissue)
- 3) **Metronidazole** is now preferred to **benzylpenicillin** as the antibiotic of choice
- 4) If vaccination history is incomplete or unknown
 - ⇒ a dose of **tetanus vaccine** should be given combined with,
 - ⇒ intramuscular human **tetanus immunoglobulin** for high-risk wounds

.....تخيّل فلاجيل يعالج التيتانوس

Tetanus vaccination

- The tetanus vaccine is a cell-free purified toxin that is normally given as part of a combined vaccine.
- **Tetanus vaccine is currently given in the UK as part of the routine immunisation schedule at:**
 - 2 months
 - 3 months
 - 4 months
 - 3-5 years
 - 13-18 years
- This therefore provides 5 doses of tetanus-containing vaccine.
- Five doses is now considered to provide adequate long-term protection against tetanus.
- Intramuscular human tetanus immunoglobulin should be given to patients with high-risk wounds (e.g. Compound fractures, delayed surgical intervention, significant degree of devitalised tissue) irrespective of whether 5 doses of tetanus vaccine have previously been given
- If vaccination history is incomplete or unknown then a dose of tetanus vaccine should be given combined with intramuscular human tetanus immunoglobulin for high-risk wounds

Botulism

- Botulism occurs either from:
 - ⇒ Gut colonisation (e.g., ingestion of contaminated home-canned food) or
 - ⇒ an infected wound
- *Clostridium botulinum* spores are widespread in soil and aquatic sediment.
- *Clostridium botulinum* produces an exotoxin that blocks acetylcholine (ACh) release leading to flaccid paralysis

Typical initial features include:

Descending weakness with autonomic dysfunction (fixed dilated pupils)

- Diplopia
 - Ptosis, Mydriasis
 - Facial weakness
 - Dysarthria, and
 - Dysphagia.
 - Later, respiratory difficulty and limb weakness occur.
- ☒ Neuromuscular blockade causes the clinical features.
- ☒ the impaired cholinergic transmission also involves autonomic synapses, causing:
- 1) Poorly reactive dilated pupils,
 - 2) dry mouth,
 - 3) paralytic ileus and
 - 4) Occasionally bradycardia.
 - 5) Reflexes are depressed or absent,
 - 6) Sensation is normal and CSF is normal in botulism.

Exotoxins and endotoxins

Exotoxins are secreted by bacteria, Endotoxins are only released following lysis of the cell

Exotoxins

- Exotoxins are generally released by **Gram positive bacteria** with the notable exceptions of *Vibrio cholerae* and some strains of *E. coli*.

There may be classified into a number of different groups:

- 1) **Superantigens** (bridges the MHC class II protein on antigen-presenting cells with the T cell receptor on the surface of T cells resulting in **massive cytokine release**)

Staphylococcus aureus exotoxins: lead to

- 1) acute gastroenteritis (enterotoxins),
- 2) toxic shock syndrome (TSST-1 superantigen) and
- 3) staphylococcal scalded skin syndrome (exfoliatin)

Streptococcus pyogenes: → scarlet fever (erythrogenic toxins)

- 2) **AB toxins - ADP ribosylating**

- **Diphtheria toxin:**
 - ⇒ inhibits protein synthesis by catalyzing ADP-ribosylation of elongation factor EF-2 causing a diphtheric membrane on tonsils caused by necrotic mucosal cells
 - ⇒ Systemic distribution may produce necrosis of myocardial, neural and renal tissue
- **Pseudomonas aeruginosa:**
 - ⇒ produces exotoxin A which also inhibits EF-2
- **cholera toxin**
 - ⇒ causes **activation of adenylate cyclase** (via G_s) leading to increases in cAMP levels, which in turn leads to increased Cl secretion and reduced Na absorption
- **pertussis exotoxin** inhibits G_i leading to increases in cAMP levels

Escherichia coli

- heat labile: **activates adenylate cyclase** (via G_s), increasing cAMP → watery diarrhoea
- heat stable: **activates guanylate cyclase**, increasing cGMP → watery diarrhoea

Bacillus anthracis

⇒ produces oedema factor, a **bacterial adenylate cyclase** which increases cAMP

Clostridium tetani neurotoxin

⇒ Tetanospasmin which blocks the release of GABA and glycine.
⇒ Causes Lockjaw

Clostridium perfringens

⇒ Produces α -toxin, a lecithinase,
⇒ Causes gas gangrene (myonecrosis) and haemolysis.

Clostridium botulinum

⇒ produces an exotoxin that blocks acetylcholine (ACh) release
⇒ leading to flaccid paralysis

Shigella dysenteriae

⇒ produces Shiga toxin which inactivates 60S ribosome

Endotoxins

- Endotoxins are lipopolysaccharides that are released from **Gram-negative** bacteria such as **Neisseria meningitidis**.

Gram Negative Rods Haemophilus influenzae

- It is a Gram negative bacillus.
- It is found in increased frequency in smokers and patients with COPD.
- A common causative agent for ventilator-associated pneumonia.
- Infection tends to occur within five days of hospital admission.

Acute epiglottitis

- Acute epiglottitis is rare but serious infection
- caused by Haemophilus influenzae type B
- Prompt recognition and treatment is essential as airway obstruction may develop.
- Epiglottitis was generally considered a disease of childhood but in the UK it is now more common in adults due to the immunisation programme.
- The incidence of epiglottitis has decreased since the introduction of the Hib vaccine

Features:

- 1) Rapid onset
 - 2) High temperature, generally unwell
 - 3) Stridor
 - 4) Drooling of saliva
- Sudden airway obstruction may occur and it is vital to obtain the assistance of an anaesthetist urgently.
 - **No attempt** should be made to visualise the epiglottis until an anaesthetist is present as there is a high risk of causing acute airway obstruction by touching the inflamed tissue.
 - The diagnosis may be confirmed on direct visualisation of a cherry-red epiglottis.
 - **Early intubation is essential**, especially in cases where there is respiratory distress.
 - Adult epiglottitis is much less common but has a higher mortality.
 - The usual causative organism is **Haemophilus influenzae type b**.

Management:

A significant number of strains are resistant to ampicillin and a **third generation cephalosporin** is the treatment of choice.

Gram Negative Rods

Escherichia coli

- A facultative anaerobic, lactose-fermenting, Gram negative rod
- A normal gut commensal
- **E. coli infections lead to a variety of diseases in humans including:**
 - 1) Diarrhoeal illnesses
 - 2) UTIs
 - 3) Neonatal meningitis

Serotypes

E. coli may be classified according to the antigens which may trigger an immune response:

Antigen	Origin	Notes
O	Lipopolysaccharide layer	
K	Capsule	Neonatal meningitis secondary to E. coli is usually caused by a serotype that contains the capsular antigen K-1
H	Flagellin	

E. coli O157:H7

- A particular strain associated with severe, bloody, watery diarrhoea.
- It has a high mortality rate and can be complicated by haemolytic uraemic syndrome.
- It is often spread by contaminated ground beef. اللحمة البقرى المفرومة

Gram Negative Rods

Salmonella

- The Salmonella group contains many members, most of which cause diarrhoeal diseases.
- They are aerobic, Gram negative rods which are not normally present as commensals in the gut.
- **Typhoid** and **paratyphoid** are caused by Salmonella typhi and Salmonella paratyphi (types A, B & C) respectively.
- They are often termed **enteric fevers**, producing systemic symptoms such as headache, fever, arthralgia

Features:

- 1) initially systemic upset: headache, fever, arthralgia
- 2) **relative bradycardia**
- 3) abdominal pain, distension
- 4) **constipation**: although Salmonella is a recognised cause of diarrhoea, constipation is more common in typhoid
- 5) **rose spots**:
 - ⇒ present on the trunk in 40% of patients
 - ⇒ more common in paratyphoid

Possible complications include

- 1) osteomyelitis:
(Especially in sickle cell disease where Salmonella is one of the most common pathogens)
- 2) GI bleed/perforation
- 3) meningitis
- 4) cholecystitis
- 5) chronic carriage (1%, more likely if adult females)

Treatment: ciprofloxacin



Rose spots

Gram Negative Rods

Shigella

- causes **bloody** diarrhoea, abdo pain
- severity depends on type:
 - ⇒ S sonnei (e.g. from UK) may be mild,
 - ⇒ S flexneri or S dysenteriae
(Produces Shiga toxin which inactivates 60S ribosome) from abroad may cause severe disease

Treatment: ciprofloxacin

Cholera

- caused by Vibrio cholerae - Gram negative bacteria

Features:

- 1) profuse 'rice water' diarrhoea
- 2) dehydration
- 3) hypoglycaemia

Management:

- 1) oral rehydration therapy
- 2) antibiotics: doxycycline, ciprofloxacin

Cat scratch disease

Caused by the Gram negative rod **Bartonella henselae**

Features:

- 1) history of a cat scratch
- 2) fever, headache, malaise
- 3) regional lymphadenopathy

Brucellosis

Gram negative aerobic coccobacilli

- Brucellosis is a zoonosis more common in the Middle East and in farmers.
- Four major species cause infection in humans: *B melitensis* (sheep), *B abortus* (cattle), *B canis* and *B suis* (pigs).
- Brucellosis has an incubation period 2 - 6 weeks

Features:

- 1) fever, malaise
- 2) hepatosplenomegaly
- 3) sacroilitis:
 - ⇒ spinal tenderness,
 - ⇒ *Brucella* affects lumbar spine (TB affects thoracic spine)
- 4) complications:
 - 1) osteomyelitis,
 - 2) infective endocarditis,
 - 3) meningoencephalitis,
 - 4) orchitis
- 5) leukopenia often seen

Diagnosis:

- 1) *Brucella* serology is the best test for diagnosis
- 2) blood and bone marrow cultures may be suitable in certain patients, but these tests are often negative
- 3) the Rose Bengal plate test can be used for screening but other tests are required to confirm the diagnosis

Management:

- doxycycline plus:
 - ⇒ streptomycin or rifampicin

Malaria

Non-falciparum Malaria

- The most common cause of non-falciparum malaria is Plasmodium **vivax**, with Plasmodium ovale and Plasmodium malariae accounting for the other cases.
- Plasmodium vivax is often found in Central America and the Indian Subcontinent
- Plasmodium ovale typically comes from Africa

Features:

- General features of malaria: fever, headache, **splenomegaly**
- Plasmodium **vivax/ovale**:
 - ☒ Cyclical fever every 48 hours.
 - ☒ have a **hypnozoite** stage and may therefore relapse following treatment
- **Plasmodium malariae**:
 - ☒ cyclical fever every 72 hours
 - ☒ associated with nephrotic syndrome

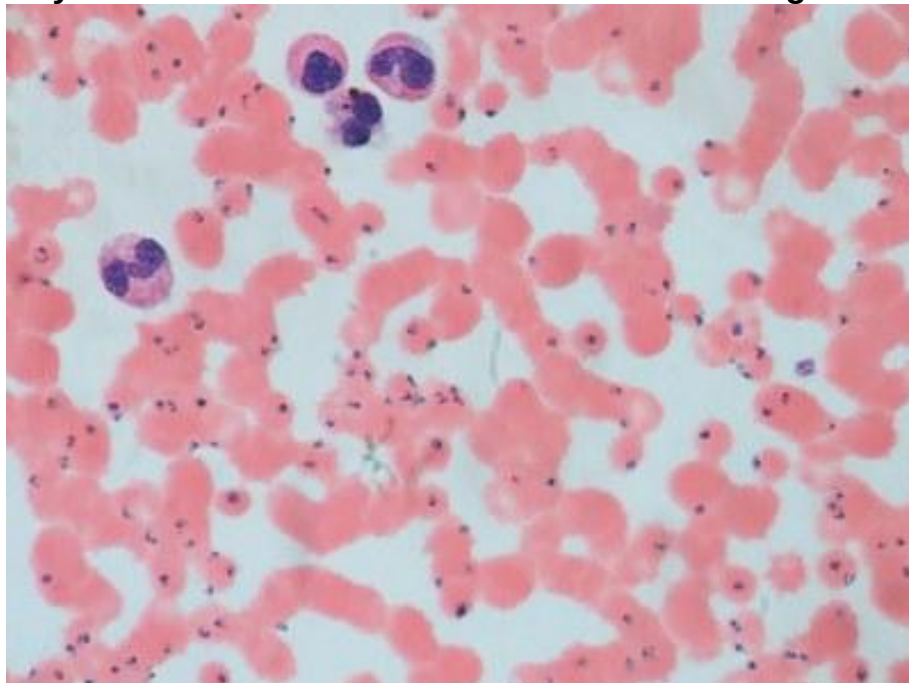
P. vivax: → the thick blood slide shows **large parasites** with **fragmented cytoplasm**
→ the thin film shows **enlarged red cells** containing **amoeboid parasites** with Schuffner's nodes

Treatment:

- 1) Non-falciparum malarias are almost always **chloroquine sensitive**
- 2) Patients with **ovale** or **vivax malaria** should be given **primaquine** following acute treatment with chloroquine to **destroy liver hypnozoites** and **prevent relapse**

Malaria Falciparum

- The incubation period for falciparum malaria is approximately 12 days.
- Chemoprophylaxis should be started one week before travelling to a malaria-endemic country and continued for one month after returning.



In the slide shown, the blood film shows **ring forms** within erythrocytes; some erythrocytes contain **two to three parasites per cell** - typical of falciparum; other forms of malaria seldom have more than one parasite per red cell.

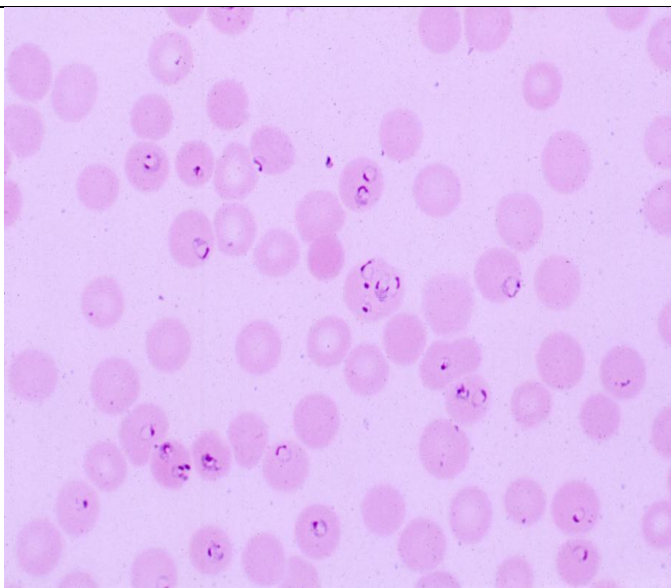
Feature of severe malaria:

- 1) schizonts on a blood film
- 2) parasitaemia > 2%
- 3) hypoglycaemia
- 4) temperature > 39 C
- 5) severe anaemia
- 6) complications as below

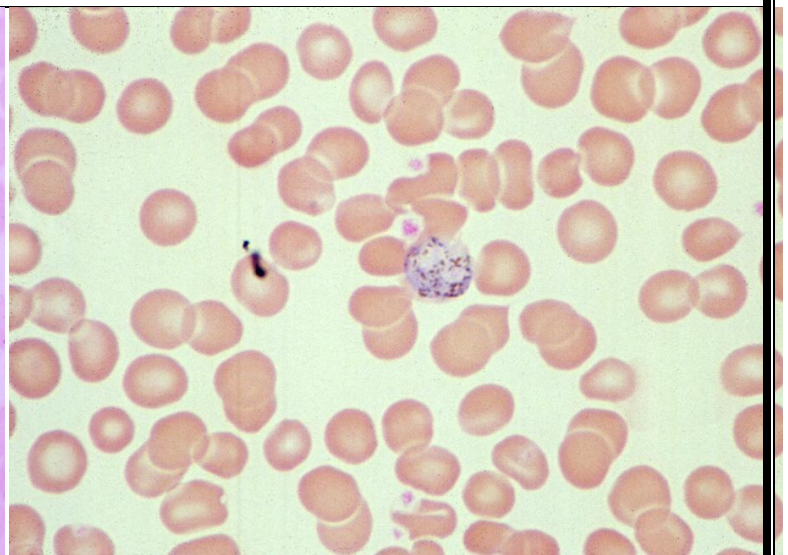
Complications:

- 1) hypoglycaemia
- 2) cerebral malaria: seizures, coma
- 3) acute renal failure: blackwater fever, **secondary to intravascular haemolysis**, mechanism unknown
- 4) acute respiratory distress syndrome (ARDS)
- 5) disseminated intravascular coagulation (DIC)

Thin film usually shows many ring forms of crescent-shaped gametocytes.



This micrograph illustrates the trophozoite form, or immature-ring form, of the malarial parasite within peripheral erythrocytes. Red blood cells infected with trophozoites do not produce sequestrins and, therefore, are able to pass through the spleen.



A mature schizont within an erythrocyte. These red blood cells (RBCs) are sequestered in the spleen when malaria proteins, called sequestrins, on the RBC surface bind to endothelial cells within that organ. Sequestrins are only on the surfaces of erythrocytes that contain the schizont form of the parasite.

Treatment of falciparum malaria:

A) Uncomplicated falciparum malaria:

- ☒ strains resistant to chloroquine are prevalent in certain areas of Asia and Africa
- ☒ the 2010 WHO guidelines recommend **artemisinin-based combination therapies (ACTs) as first-line therapy**

Examples include:

- ⇒ **artemether** plus lumefantrine,
- ⇒ **artesunate** plus
 - ☒ amodiaquine, or
 - ☒ mefloquine, or
 - ☒ sulfadoxine-pyrimethamine,
- ⇒ **dihydroartemisinin** plus piperaquine

B) Severe falciparum malaria:

- 1) **If parasite counts of more than 2%:**
 - ⇒ will usually need parenteral treatment irrespective of clinical state
 - ⇒ **intravenous artesunate** is now recommended by WHO in preference to intravenous quinine
- 2) **If parasite count > 10%:**
 - ⇒ **exchange transfusion** should be considered
- 3) **shock** may indicate **coexistent bacterial septicaemia** - **malaria rarely** causes haemodynamic collapse

Malaria prophylaxis:

- There are around 1,500 - 2,000 cases /year of malaria in patients returning from endemic countries.
- The majority of these cases (around 75%) are caused by the potentially fatal *Plasmodium falciparum* protozoa.
- The majority of patients who develop malaria did not take prophylaxis.
- It should also be remembered that UK citizens who originate from malaria endemic areas quickly lose their innate immunity.

Up-to-date charts with recommended regimes for malarial zones should be consulted prior to prescribing

Drug	Side-effects + notes	Time to begin before travel	Time to end after travel
Atovaquone + proguanil (Malarone)	GI upset	1 - 2 days	7 days
Doxycycline	1) Photosensitivity 2) Oesophagitis	1 - 2 days	4 weeks
Chloroquine	1) Headache 2) Contraindicated in epilepsy 3) Taken weekly	1 week	4 weeks
Proguanil (Paludrine)		1 week	4 weeks
Proguanil + chloroquine	See above	1 week	4 weeks
Mefloquine (Lariam)	1) Dizziness 2) Neuropsychiatric disturbance 3) Contraindicated in epilepsy 4) Taken weekly	2 - 3 weeks	4 weeks

Doxycycline prophylaxis is safe option with less resistance in many parts of the world

Pregnant women:

- Should be advised to avoid travelling to regions where malaria is endemic
- Diagnosis can also be difficult as parasites may not be detectable in the blood film due to placental sequestration.
- **However, if travel cannot be avoided:**
 - 1) chloroquine can be taken
 - 2) proguanil: folate supplementation (5mg od) should be given
 - 3) Malarone (atovaquone + proguanil): the BNF advises to **avoid** these drugs unless essential, If taken then folate supplementation should be given
 - 4) mefloquine: caution advised
 - 5) doxycycline is contraindicated

Children:

- It is again advisable to avoid travel to malaria endemic regions with children if avoidable.
- However, if travel is essential then children should take malarial prophylaxis as they are more at risk of serious complications.
 - 1) **Diethyltoluamide** (DEET) 20-50% can be used in children over 2 months of age
 - 2) doxycycline is only licensed in the UK for children over the age of 12 years
- DEET: (yellow [OIL](#)) It is the most common active ingredient in [insect repellents](#).
- It is intended to be applied to the [skin](#) or to [clothing](#)
- Provides protection against [mosquitos](#), [ticks](#), [fleas](#), [chiggers](#), [leeches](#), and many other biting insects.

Leptospirosis

داء اللولبية النحيفة

- Also known as **Weil's disease***,
- Commonly seen in questions referring to sewage workers عمال الصرف الصحي, farmers, vets الأطباء البيطريون or people who work in abattoir مسلخ مجزر.
- It is caused by the spirochaete *Leptospira interrogans* (serogroup L ictero-haemorrhagiae),
- Classically being spread by contact with **infected rat urine**.
- Weil's disease should always be considered in high-risk patients with **hepatorenal failure**

Features:

- 1) fever
- 2) flu-like symptoms
- 3) **subconjunctival haemorrhage**
- 4) **jaundice**
- 5) **renal failure (50% of patients)**
- 6) headache, may herald ينذر the onset of meningitis

Management high mortality –ICU admission

- high-dose **benzylpenicillin** or **doxycycline**

*the term Weil's disease is sometimes reserved for the most severe 10% of cases that are associated with jaundice

Q fever

- a rickettsial zoonotic disease
- Caused by *Coxiella burnetii*.
- Q fever is usually a self-limited respiratory illness due to the inhalation of infected aerosols, especially from **animal products**.
- The source of infection is typically an abattoir مسلخ مجزر, cattle/sheep

Features:

- 1) typically prodrome: fever, malaise,
- 2) **thrombocytopenia**
- 3) causes pyrexia of unknown origin,
- 4) atypical pneumonia,
- 5) endocarditis (culture negative)
- 6) hepatitis
- 7) osteomyelitis
- 8) Immune complex GN
- 9) Microscopic haematuria may be present.
- 10) **Arterial emboli**.

Diagnosis:

- ☒ The diagnosis is best made **serologically**
- ☒ a phase I antibody titre to *Coxiella burnetii* (IgG and/or IgA) greater than 1:200 is virtually diagnostic of Q fever endocarditis

Laboratory tests often show:

- 1) Hepatitis
- 2) Anaemia
- 3) Elevated ESR
- 4) Thrombocytopenia and
- 5) Hypergammaglobulinaemia.

Management:

⇒ **Doxycycline**

Q fever **FUO**, **atypical pneumonia**, **culture negative endocarditis** اللهو الخفى

- In Q fever endocarditis, the aortic valve is involved in over 80% of cases.
- A murmur is not always present, but augmentation of an existing murmur may occur.
- Low-grade fever (or no fever), signs of heart failure, hepatosplenomegaly, clubbing, arterial emboli, and leukocytoclastic vasculitic rash may also be present.

Lyme disease

- Caused by the **spirochaete *Borrelia burgdorferi*** and is spread by ticks
- There are several phases to Lyme disease;

The first Phase:

- 1) **Erythema chronicum migrans** اهم حاجة
 - ⇒ Small papule often at site of the tick bite (axilla, groin , thigh)
 - ⇒ which develops into a larger annular lesion with central clearing, '**bull's-eye**'
 - ⇒ Occurs in 70% of patients
- 2) Systemic symptoms: **FLU-like**: malaise, fever, arthralgia, headache and neck stiffness.

The second phase

- Normally occurs between **1 - 6 months** after infection and
- presents as:
 - ☒ Meningitis,
 - ☒ **multiple cranial** or peripheral neuropathies, or
 - ☒ An acute polyneuropathy **resembling Guillain-Barré syndrome**.

Stage three of the disease

- Occurs **months** to **years** after infection and
- presents as:
 - ☒ a chronic myelitis,
 - ☒ encephalopathy or
 - ☒ demyelinating disorder.

Investigation:

- 1) serology: **antibodies to *Borrelia burgdorferi***
- 2) CSF: reveals a **lymphocytic pleocytosis** with **intrathecal oligoclonal band** production.

(NB. In Guillain-Barré syndrome normal cell count in csf)

Management:

- 1) **Doxycycline** if early disease.
- 2) **Amoxicillin** is an alternative if doxycycline is contraindicated (e.g. pregnancy)
- 3) **ceftriaxone** if disseminated disease

Jarisch-Herxheimer reaction: (also seen in syphilis)

- ⇒ sometimes seen after initiating therapy
- ⇒ fever, rash, tachycardia after first dose of antibiotic
- ⇒ more commonly seen in syphilis, (another spirochaetal disease)

Neuroborreliosis (Lyme disease) *Borrelia burgdorferi*

Intracellular

Legionella

- Legionnaire's disease is caused by the intracellular bacterium "Legionella pneumophila".
- It typically colonizes water tanks and hence questions may hint at air-conditioning systems or foreign holidays.
- Person-to-person transmission is not seen

Features:

- 1) flu-like symptoms including fever (present in > 95% of patients)
- 2) dry cough
- 3) relative **bradycardia** (Typhoid افتر)
- 4) confusion
- 5) **lymphopaenia**
- 6) **hyponatraemia** (SIADH),
- 7) renal failure
- 8) deranged liver function tests
- 9) pleural effusion: seen in around 30% of patients

Progresses to bilateral involvement in 50% of cases

Diagnosis:

- **urinary antigen**

Management:

- 1) Monotherapy:
 - ⇒ **The newer quinolones** (especially **levofloxacin**) and
 - ⇒ **The newer macrolides** (especially **azithromycin**) are effective for treating legionellosis.
 - ☒ In comparison with erythromycin, they are more potent, better tissue penetration and significantly less GIT toxicity.
- 2) **Rifampin** combined with **erythromycin**, combination therapy is now only recommended in patients who are failing standard therapy.

Intracellular

Chlamydia

- Chlamydia is the most prevalent sexually transmitted infection in the UK
- Caused by Chlamydia trachomatis, an obligate intracellular pathogen.
- Approximately 1 in 10 young women in the UK have Chlamydia.
- The incubation period is around 7-21 days,
- a large percentage of cases are asymptomatic

Features:

- 1) asymptomatic in around 70% of women and 50% of men
- 2) women: cervicitis (discharge, bleeding), dysuria
- 3) men: urethral discharge, dysuria

Potential complications:

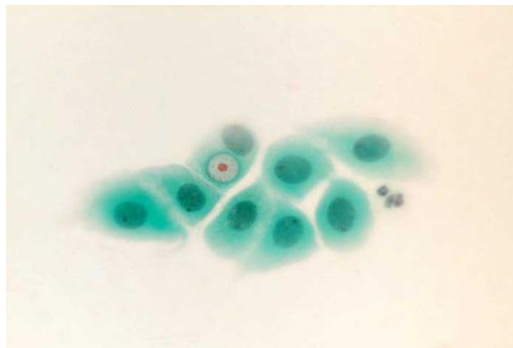
- 1) Epididymitis
- 2) Pelvic inflammatory disease
- 3) Endometritis
- 4) Increased incidence of ectopic pregnancies
- 5) Infertility
- 6) Reactive arthritis
- 7) Perihepatitis (**Fitz-Hugh-Curtis syndrome**)

Investigation:

- 1) **Nuclear Acid Amplification Tests** (NAATs) are now rapidly emerging as
 - ☒ The **investigation of choice**.
 - ☒ It has sensitivities of around **90-95%**. It can also run many samples easily.
 - ☒ urine (first void urine sample), vulvovaginal swab or cervical swab may be tested using the NAAT technique
- 2) traditional cell culture is no longer widely used

Screening:

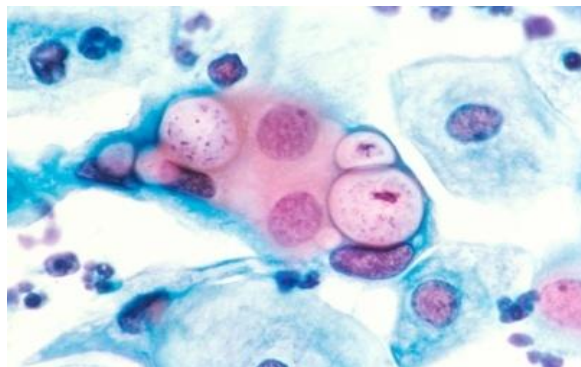
- in England the National Chlamydia Screening Programme is open to all men and women aged 15-24 years
- the 2009 SIGN guidelines support this approach, suggesting screening all sexually active patients aged 15-24 years
- relies heavily on opportunistic testing



Pap smear demonstrating infected endocervical cells. Red inclusion bodies are typical

Management

- 1) **Doxycycline** (7 day course) or **azithromycin** (single dose).
 - ⇒ The 2009 SIGN guidelines suggest **azithromycin should be used first-line** due to potentially poor compliance with a 7 day course of doxycycline
- 2) If pregnant then
 - ⇒ **Erythromycin** or **amoxicillin** may be used.
 - ⇒ The SIGN guidelines suggest **considering azithromycin 'following discussion of the balance of benefits and risks with the patient'**
- 3) patients diagnosed with Chlamydia:
 - ⇒ should be offered a choice of provider for initial partner notification - either trained practice nurses with support from GUM, or referral to GUM
- 4) for men with symptomatic infection:
 - ⇒ all partners from the four weeks prior to the onset of symptoms should be contacted
- 5) for women and asymptomatic men:
 - ⇒ all partners from the last six months or the most recent sexual partner should be contacted
- 6) contacts of confirmed Chlamydia cases should be offered treatment prior to the results of their investigations being known (treat then test)



Another Pap smear demonstrating infected endocervical cells. Stained with H&E

Vaginal discharge

Vaginal discharge is a common presenting symptom and is not always pathological

Common causes:

- 1) physiological
- 2) Candida
- 3) Trichomonas vaginalis
- 4) bacterial vaginosis

Less common causes:

- 1) whilst cervical infections such as Chlamydia and Gonorrhoea can cause a vaginal discharge this is rarely the presenting symptoms
- 2) ectropion
- 3) foreign body
- 4) cervical cancer

Key features of the common causes:

Condition	Key features
Candida	• Cottage cheese discharge • Vulvitis • Itch
Trichomonas vaginalis anaerobic protozoan TTT Metronidazole	• Discharge: ⇒ Offensive, yellow/green, frothy, ⇒ PH > 6.5 • Vulvovaginitis • Strawberry cervix
Bacterial vaginosis	Offensive, thin, white/grey, 'fishy' discharge

Bacterial vaginosis

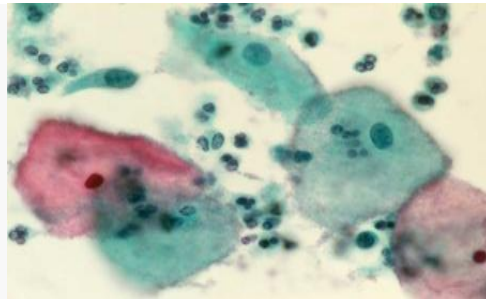
- Bacterial vaginosis (BV) describes an overgrowth of predominately **anaerobic** organisms such as **Gardnerella vaginalis**.
- This leads to a consequent fall in lactic acid producing aerobic lactobacilli resulting in a raised vaginal pH.
- Whilst BV is not a STI it is seen almost exclusively in sexually active women.

Features:

- 1) vaginal discharge: '**fishy**', offensive
- 2) asymptomatic in 50%

Amsel's criteria for diagnosis of BV - 3 of 4 points should be present

- 1) thin, white homogenous discharge
- 2) vaginal pH > 4.5
- 3) positive whiff test (addition of **potassium hydroxide** results in **fishy odour**)
- 4) clue cells on microscopy مهمه جدا



Clue cells - epithelial cells develop a stippled appearance due to being covered with bacteria

Management:

- 1) oral **metronidazole** for 5-7 days
 - ☒ 70-80% initial cure rate
 - ☒ relapse rate > 50% within 3 months
- 2) the BNF suggests **topical metronidazole** or **topical clindamycin** as alternatives

Bacterial vaginosis in pregnancy

- results in an increased risk of preterm labour, low birth weight and chorioamnionitis, late miscarriage
- It was previously taught that oral metronidazole should be avoided in the first trimester and **topical clindamycin** used instead.
- Recent guidelines however recommend that oral metronidazole is used throughout pregnancy.
- The BNF still advises against the use of high dose metronidazole regimes

Pelvic inflammatory disease

- Pelvic inflammatory disease (PID) is a term used to describe infection and inflammation of the female pelvic organs including the uterus, fallopian tubes, ovaries and the surrounding peritoneum.
- It is usually the result of ascending infection from the endocervix

Causative organisms:

- 1) **Chlamydia trachomatis** - the most common cause
- 2) **Neisseria gonorrhea**
- 3) **Mycoplasma genitalium**
- 4) **Mycoplasma hominis**

Features:

- 1) Lower abdominal pain
- 2) Fever
- 3) Deep dyspareunia
- 4) Dysuria and menstrual irregularities may occur
- 5) Vaginal or cervical discharge
- 6) Cervical excitation

Investigation:

- screen for Chlamydia and Gonorrhoea

Management:

- 1) due to the difficulty in making an accurate diagnosis, and the potential complications of untreated PID, consensus guidelines recommend having a low threshold for treatment
 - ☒ **oral ofloxacin + oral metronidazole** or
 - ☒ **intramuscular ceftriaxone + oral doxycycline + oral metronidazole**
- 2) IUD Removal:
 - ⇒ RCOG guidelines suggest that in mild cases of PID -> IUD may be left in.
 - ⇒ The more recent BASHH guidelines suggest that the evidence is limited but that 'Removal of the IUD should be considered and may be associated with better short term clinical outcomes'

Complications:

- 1) infertility - the risk may be as high as 10-20% after a single episode
- 2) chronic pelvic pain
- 3) ectopic pregnancy

Clindamycin is used in the treatment of *Mycoplasma hominis*. *Mycoplasma hominis* is one of the most frequently isolated mycoplasma in the genital tract. It is an opportunistic pathogen which may cause pelvic inflammatory disease in immunocompromised patients.

Epididymo-orchitis

- Describes an infection of the **epididymis** +/- **testes** resulting in pain and swelling.
- It is most commonly caused by local spread of infections from:
 - ⇒ The genital tract (such as Chlamydia trachomatis and Neisseria gonorrhea) or
 - ⇒ The bladder.

The most important differential diagnosis is **testicular torsion**.

This needs to be **excluded urgently** to prevent **ischaemia** of the testicle.

Features:

- 1) unilateral testicular pain and swelling
- 2) urethral discharge may be present, but urethritis is often asymptomatic

Management:

- 1) the British Association for Sexual Health and HIV (BASHH) produced guidelines in 2010
- 2) if the organism is unknown BASHH recommend:
 - **Ceftriaxone 500mg IM** single dose, plus
 - **doxycycline 100mg** by mouth twice daily for 10-14 days
- 3) further investigations following treatment are recommended to exclude any underlying structural abnormalities

Factors suggesting **testicular torsion** include:

- 1) patients < 20 years,
- 2) severe pain and an
- 3) acute onset

Non-gonococcal urethritis (NGU)

- The incubation period is 7- 21 days
- Patients often present with a thin colourless discharge and absence of bacteria on urethral swab.
- The treatment for NGU is **doxycycline 100 mg** twice a day for 7 days **OR** **azithromycin 1 g stat**.
- Erythromycin is second line.

Gonococcal urethritis

- Incubation period of 1-5 days on average
- Causes a purulent discharge.
- Management options for gonococcus include
- **Ceftriaxone 500 mg IM** as a **single dose** with **azithromycin 1 g oral** as a **single dose**.

Genital Ulcers

A) Genital herpes:

- ✗ most often caused by the herpes simplex virus (HSV) type 2 (Cold sores are usually due to HSV type 1)
- ✗ Primary attacks are often severe and associated with fever
- ✗ subsequent attacks are generally less severe and localised to one site

TTT:

- ⇒ oral aciclovir,
- ⇒ some patients with frequent exacerbations may benefit from longer term aciclovir

B) Chancroid:

- ✗ A tropical disease caused by *Haemophilus ducreyi*.
- ✗ It causes **painful** genital ulcers associated with unilateral, **painful** inguinal lymph node enlargement.
- ✗ The ulcers typically have a sharply defined, ragged, undermined border.

C) Syphilis:

- ✗ A sexually transmitted infection caused by the **spirochaete *Treponema pallidum***.
- ✗ Infection is characterised by primary, secondary and tertiary stages.
- ✗ A **painless** ulcer (chancre) is seen in the primary stage.
- ✗ local **non-tender** lymphadenopathy
- ✗ The incubation period= 9-90 days

D) Lymphogranuloma venereum (LGV)

- ✗ caused by *Chlamydia trachomatis*
- ✗ Typically infection comprises of three stages
 - stage 1: small **painless** pustule which later forms an ulcer
 - stage 2: **painful** inguinal lymphadenopathy
 - stage 3: proctocolitis
- ✗ TTT: **Doxycycline**.

E) Granuloma inguinale: *Klebsiella granulomatis*

Other causes of genital ulcers

- 1) Behcet's disease
- 2) carcinoma

Painful: Chancroid, HSV

Painless: Chancre, LGV

Syphilis

- a sexually transmitted infection , caused by the spirochaete *Treponema pallidum*
- Infection is characterised by primary, secondary and tertiary stages.
- The incubation period is between 9-90 days

Primary features:

- 1) chancre - **painless** ulcer at the site of sexual contact
 - 2) local **non-tender** lymphadenopathy
- ☒ often not seen in women (the lesion may be on the cervix)

Secondary features - occurs 6-10 weeks after primary infection

- 1) fevers, lymphadenopathy
- 2) rash on trunk, palms and soles
- 3) buccal 'snail track' ulcers (30%)
- 4) condylomata lata 30%



Classical palm lesions of secondary syphilis



More generalised rash of secondary syphilis

Tertiary features

- ☒ Usually presents up to 20 years after the primary infection.
- ☒ It is divided into:
- Gummatous syphilis
 - Cardiovascular syphilis (aortic aneurysms), and
 - Late neurosyphilis. (general paralysis of the insane)
 - tabes dorsalis

Late neurosyphilis (general paralysis of the insane):

Clinical features include:

- Gradual onset confusion
- Hallucinations
- Tremors
- Fits
- Cognitive impairment
- Hyperreflexia, and
- Argyll-Robertson pupils.

- ❌ Meningovascular syphilis is a form of early neurosyphilis involving the small and medium sized intracranial vessels. It most commonly presents as a stroke involving the middle cerebral artery.

Features of congenital syphilis

- 1) blunted upper incisor teeth
- 2) keratitis
- 3) saber shins
- 4) saddle nose
- 5) deafness

Condylomata lata: الأورام اللقمية

- Wart like lesions on the genitals.
- Occurs in about one third of patients and is characterized by painless, mucosal, and warty erosions.
- They tend to develop in warm, moist sites of genitals and perineum.
- These lesions hold a high accumulation of spirochetes and are highly infectious.
- Complete resolution of the lesions is spontaneous and occurs after a few days to many weeks where it is either resolved completely or enters the tertiary phase, defined by a latent state

Investigation:

- Treponema pallidum is a very sensitive organism and cannot be grown on artificial media.
- The diagnosis is therefore usually based on clinical features, serology and microscopic examination of infected tissue (darkfield microscopy of secretions from the ulcer)
- **Serological tests can be divided into**
 - treponemal specific antibody tests
 - cardiolipin tests (not treponeme specific)

A) Treponemal specific antibody tests

- example: **TPHA** (Treponema pallidum HaemAgglutination test)
- **remains positive after treatment**

B) Cardiolipin tests:

- syphilis infection leads to the production of non-specific antibodies that react to cardiolipin
- examples include **VDRL** (Venereal Disease Research Laboratory) & **RPR** (rapid plasma reagin)
 - ❌ Sensitive in early syphilis
 - ❌ insensitive in late syphilis
 - ❌ becomes negative after treatment

Causes of false **positive** cardiolipin tests

- 1) pregnancy
- 2) SLE, anti-phospholipid syndrome
- 3) TB, leprosy
- 4) malaria
- 5) HIV

Management:

- 1) **Benzylpenicillin** benzathine penicillin 2.4 million units given intramuscularly. This is administered either as a single dose or two doses given one week apart.
 - 2) alternatives: **doxycycline**
- ☒ The **Jarisch-Herxheimer reaction** (also seen in lyme)
- ⇒ starting within 12 hours of the first dose of treatment and resolving within 24 hours
 - ⇒ **Fever, rash, tachycardia** after first dose of antibiotic.
 - ⇒ It is thought to be due to the release of endotoxins following bacterial death and typically occurs within a few hours of treatment.
 - ⇒ A **single dose of benzathine penicillin** should cure most cases of early syphilis, thus no further antibiotics should be necessary.
 - ⇒ 50% with primary syphilis, 90% with secondary syphilis and 25% with early latent syphilis. It is very rare in late syphilis but may be dangerous if there are lesions around important anatomical sites (for example, SA node, larynx).

Gastroenteritis

- Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea)

Travellers' diarrhoea:

- defined as at least 3 loose to watery stools in 24 hours with or without one or more of:
 - 1) Abdominal cramps,
 - 2) fever, nausea, vomiting or
 - 3) Blood in stool.
- The most common cause is *Escherichia coli*

Acute food poisoning:

- Describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin.
- Typically caused by *Staph aureus*, *Bacillus cereus* or *Clostridium perfringens*.

Stereotypical histories

Infection	Typical presentation
<i>Escherichia coli</i>	- Common amongst travelers - Watery stools - Abdominal cramps and nausea
Amoebiasis	- Gradual onset bloody diarrhoea, - abdominal pain and tenderness which may last for several weeks
Giardiasis	Prolonged, non-bloody diarrhoea , Abdominal cramps
Cholera	- Profuse, watery diarrhea - Severe dehydration resulting in weight loss - Not common amongst travelers
Shigella	- Bloody diarrhoea, - Vomiting and abdominal pain
<i>Staphylococcus aureus</i> S—S---S	- Severe vomiting - Short incubation period
<i>Campylobacter</i>	- A flu-like prodrome is usually followed by crampy abdominal pains, - fever and diarrhoea which may be bloody - Complications include Guillain-Barre syndrome - Reiter s syndrome (cannot pee ,cannot see ,cannot climb the tree)
<i>Bacillus cereus</i>	- Two types of illness are seen: 1) vomiting within 6 hours, stereotypically due to rice 2) diarrhoeal illness occurring after 6 hours - associated with chinese food

Incubation period:

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- 1-6 hrs: *Staph. aureus*, *Bacillus cereus* vomiting subtype ,
- Bacillus cereus* diarrhoeal illness IP of 6-14 hrs
- 12-48 hrs: *Salmonella*, *E. coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: *Giardiasis*, *Amoebiasis*

- **Enterotoxigenic *Escherichia coli* (ETEC)** is the commonest cause worldwide of TRAVELLER'S diarrhoea, incubation period is very short between 12 - 24 hours.
- **Enterohaemorrhagic E Coli (EHEC)** is a cause of bloody diarrhoea, incubation period is between 5 - 7 days.

Giardiasis

- Giardiasis is caused by the flagellate protozoan *Giardia lamblia*.
- It is spread by the faeco-oral route

Features:

- 1) often asymptomatic
- 2) Abdominal cramps, bloating and flatulence accompanied by yellow, frothy, greasy and offensive-smelling diarrhoea (steatorrhoea).
- 3) Fever and vomiting are less usual.
- 4) non-bloody diarrhoea
- 5) **chronic diarrhoea, malabsorption** and lactose intolerance can occur
- 6) stool microscopy for trophozoite and cysts are classically negative, therefore:
 - ⇒ duodenal fluid aspirates or
 - ⇒ **'string tests'** (fluid absorbed onto swallowed string خيط) are sometimes needed

Treatment: Metronidazole

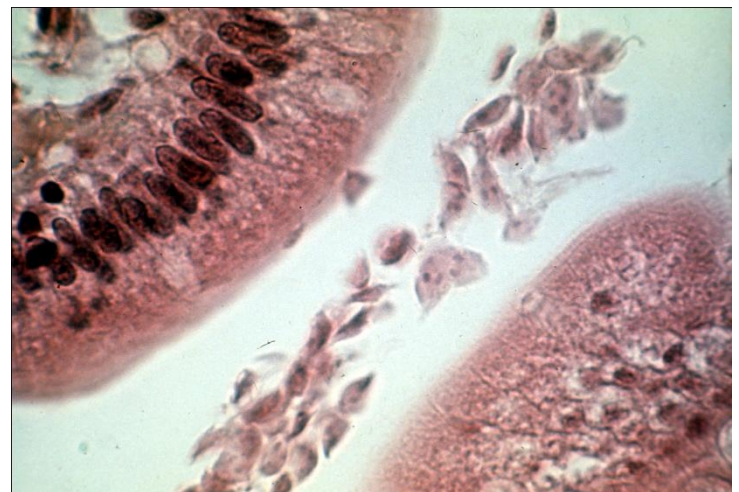
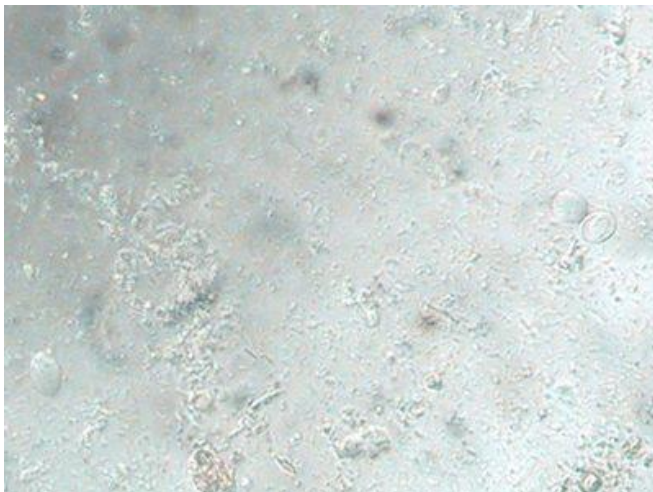


Image 1 The wet mount slide shows cysts of *Giardia intestinalis*. At higher magnification you would be able to see the characteristic double nuclei in each cyst
 Image 2 *Giardia* are clearly seen in the lumen of the bowel.

Campylobacter

Campylobacter is the commonest bacterial cause of infectious intestinal disease in the UK. The majority of cases are caused by the Gram-negative bacillus *Campylobacter jejuni*. It is spread by the faecal-oral route and has an incubation period of 1-6 days.

Features

- prodrome: headache malaise
- diarrhoea: often bloody
- abdominal pain

Management

- usually self-limiting
- the BNF advises treatment if severe or the patient is immunocompromised. Clinical Knowledge summaries also recommend antibiotics if severe symptoms (high fever, bloody diarrhoea, or more than eight stools per day) or symptoms have last more than one week
- the first-line antibiotic is clarithromycin

Complications:

- 1) Guillain barre syndrome
- 2) reiter syndrome
- 3) septicaemia, endocarditis, arthritis

Animal bites

- The majority of bites seen in everyday practice involve dogs and cats.
- These are generally polymicrobial but the most common isolated organism is *Pasteurella multocida*.

Management:

- 1) cleanse wound
 - 2) current BNF recommendation is **co-amoxiclav**
 - 3) if penicillin-allergic then **doxycycline** + **metronidazole** is recommended
- =====

Urinary tract infection in adults

Management:

A) Lower urinary tract infections in non-pregnant women:

- local antibiotic guidelines should be followed if available
- 2012 SIGN guidelines recommend **trimethoprim** or **nitrofurantoin** for **3 days**

B) Pregnant women with symptomatic bacteriuria:

- ⇒ should be treated with an antibiotic for 7 days
- ⇒ A urine culture should be sent.

C) For asymptomatic pregnant women:

- a urine culture should be performed routinely at the first antenatal visit
- if positive, a second urine culture should be sent to confirm the presence of bacteriuria
- SIGN recommend to treat asymptomatic bacteriuria detected during pregnancy with an antibiotic
- a 7 day course of antibiotics should be given
- a further urine culture should be sent following completion of treatment as a test of cure

D) For patients with sign of acute pyelonephritis:

- hospital admission should be considered
- local antibiotic guidelines should be followed if available
- the BNF currently recommends a broad-spectrum **cephalosporin** or a **quinolone** for 10-14 days

Otitis externa

Otitis externa is a common reason for primary care attendance in the UK.

Causes:

- 1) Infection:
 - ✓ Bacterial (Staphylococcus aureus, Pseudomonas aeruginosa) or
 - ✓ Fungal
- 2) Seborrhoeic dermatitis
- 3) Contact dermatitis (allergic and irritant)

Features:

- 1) Ear pain, itch, discharge
- 2) Otoscopy: red, swollen, or eczematous canal

The recommend initial management of otitis externa is:

- 1) Topical antibiotic or a combined topical antibiotic with steroid
- 2) If the tympanic membrane is perforated aminoglycosides are traditionally not used*
- 3) If there is canal debris then consider removal
- 4) If the canal is extensively swollen then an ear wick فتيل الاذن is sometimes inserted

*many ENT doctors disagree with this and feel that concerns about ototoxicity are unfounded

Second line options include

- 1) Consider contact dermatitis secondary to neomycin
- 2) Oral antibiotics if the infection is spreading
- 3) Empirical use of an antifungal agent
- 4) Taking a swab inside the ear canal

Malignant otitis externa:

- More common in elderly diabetics.
- In this condition there is extension of infection into the bony ear canal and the soft tissues deep to the bony canal.
- Intravenous antibiotics may be required.

Viral Infections

Herpes simplex virus

- There are two strains of the herpes simplex virus (HSV) in humans: HSV-1 and HSV-2.
- Whilst it was previously thought HSV-1 accounted for oral lesions (cold sores) and HSV-2 for genital herpes it is now known there is considerable overlap
- Transmission can occur in the absence of lesions
- Herpes simplex vesicles never follow a particular dermatome.

Features:

- 1) primary infection: may present with a severe gingivostomatitis
- 2) cold sores
- 3) Painful genital ulceration (60% of primary cases are asymptomatic).

Management:

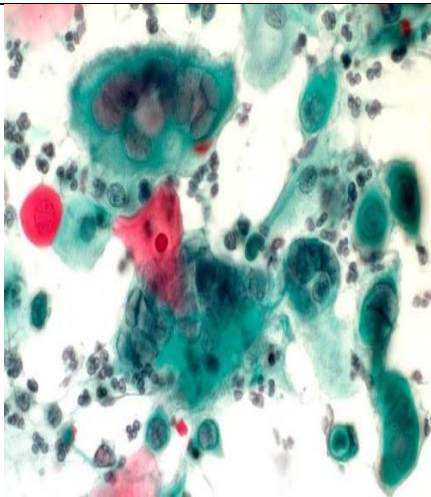
1) **Gingivostomatitis:**

- ⇒ oral aciclovir,
- ⇒ chlorhexidine mouthwash

2) **Cold sores:** topical aciclovir although the evidence base for this is modest

3) **Genital herpes:**

- ⇒ oral aciclovir
- ⇒ Some patients with frequent exacerbations may benefit from longer term aciclovir



Pap smear. Multinucleated giant cells representing infection by the herpes simplex virus. Note the 3 M's; Multinucleation, Margination of the chromatin, Molding of the nuclei



Further Pap smear showing the cytopathic effect of HSV (multi-nucleation, ground glass & margined chromatin)

HSV1

HSV2

HHV3 = (VZV)

HHV4 = (EBV)

HHV5 = (CMV)

Dendritic ulcers

Dendritic ulcers are caused by herpes simplex virus.

Presentation is usually with:

- Pain
- Photophobia
- Blurred vision
- Conjunctivitis
- Chemosis.

Steroid eye drops are contraindicated as they may induce massive amoeboid ulceration and blindness.

Diagnosis is by instillation of fluorescein eye drops which stain the ulcer (shown in slide).



TTT:

Acyclovir eye drops

Chickenpox (VZV)

(HHV-3)

- VZV is known by many names, including chickenpox virus الجدري, varicella virus, zoster virus, and human herpes virus type 3 (HHV-3).
- Herpes zoster usually has a prodrome pain before the vesicles appear.
- It usually follows a particular dermatome but in immune suppression the disease may affect more than one dermatome.
- Chickenpox (varicella) is caused by primary infection with varicella zoster virus.
- Shingles is reactivation of dormant virus in dorsal root ganglion
- **Chickenpox is highly infectious:**
 - ⇒ spread via the **respiratory route**
 - ⇒ can be caught from someone with shingles
 - ⇒ infectivity = 4 days before rash, until 5 days after the rash first appeared*
 - ⇒ incubation period = 10-21 days

*it was traditionally taught that patients were infective until all lesions had scabbed over



Clinical features: (tend to be more severe in older children/adults)

- 1) Fever initially
- 2) Itchy rash:
 - ⇒ Initially macular then papular then vesicles and blisters over an erythematous base in a dermatomal distribution.
 - ⇒ starting on head/trunk before spreading
- 3) systemic upset is usually mild

Management: is supportive

- 1) keep cool, trim nails
- 2) calamine lotion
- 3) School exclusion:
 - ⇒ current HPA advice is 5 days from start of skin eruption
 - ⇒ They also state 'Traditionally children have been excluded until all lesions are crusted. However, transmission has never been reported beyond the fifth day of the rash.'

4) Immunocompromised patients and newborns with peripartum exposure:

- ⇒ should receive varicella zoster **immunoglobulin** (VZIG)
- ⇒ If chickenpox develops then **IV aciclovir** should be considered

☒ A common complication is secondary bacterial infection of the lesions.

☒ Rare complications include:

- pneumonia
- encephalitis (cerebellar involvement may be seen)
- disseminated haemorrhagic chickenpox
- arthritis, nephritis and pancreatitis may very rarely be seen

☒ Shingles is uncommon in individuals under 35 years of age; a history of shingles under this age, especially recurrent episodes, is highly suggestive of HIV infection.



The slide shows the typical rash of chickenpox.

Varicella pneumonia occurs in up to 20% of adults with chickenpox, appearing three to five days into the course of the illness.

Symptoms include:

- Tachypnoea
- Cough
- Dyspnoea, and
- Fever.

Cyanosis, pleuritic chest pain and haemoptysis are common.

Chest x ray shows patchy shadowing.

About 30 young adults die each year from varicella pneumonia. They are best managed on a high-dependency unit



The slide shows the typical rash of chickenpox



The slide shows the typical rash of herpes zoster (shingles), caused by VZV.

Chickenpox exposure in pregnancy

- In pregnancy there is a risk to both the mother and also the fetus, a syndrome now termed **fetal varicella syndrome**

Fetal varicella syndrome (FVS):

- risk of FVS following maternal varicella exposure is around 1% if occurs before 20 weeks gestation
- studies have shown a very small number of cases occurring between 20-28 weeks gestation and none following 28 weeks

Features of FVS include:

- 1) Skin scarring,
- 2) eye defects (microphthalmia),
- 3) microcephaly,
- 4) limb hypoplasia and
- 5) learning disabilities

Management of chickenpox exposure:

- 1) if there is any doubt about the mother previously having chickenpox maternal blood should be checked for varicella antibodies
 - ⇒ If the pregnant woman is **not immune** to varicella:
 - ☒ She should be given **varicella zoster immunoglobulin (VZIG)** as soon as possible.

RCOG and Greenbook guidelines suggest VZIG is effective up to 10 days post exposure

- 2) consensus guidelines suggest **oral aciclovir** should be given if pregnant women with chickenpox present within 24 hours of onset of the rash

Ramsay Hunt syndrome

Ramsay Hunt syndrome (herpes zoster oticus) is caused by the reactivation of the varicella zoster virus in the geniculate ganglion of **the seventh cranial nerve**.

Features:

- 1) **auricular pain** is often **the first feature**
- 2) facial nerve palsy
- 3) vesicular rash around the ear
- 4) other features include vertigo and tinnitus

Management:

- **oral aciclovir** and **corticosteroids** are usually given

Reye's syndrome

- Reye's syndrome is a severe, **progressive encephalopathy** affecting children that is accompanied by **fatty infiltration of the liver**, **kidneys** and **pancreas**.
- The aetiology of Reye's syndrome is not fully understood although there is a known association with **aspirin** use and a viral cause has been postulated
- The peak incidence is 2 years of age,

Features include:

- 1) may be history of preceding viral illness
- 2) encephalopathy: confusion, seizures, cerebral oedema, coma
- 3) fatty infiltration of the liver, kidneys and pancreas
- 4) hypoglycaemia

Management is supportive

Although the prognosis has improved over recent years there is still a mortality rate of 15-25%

Epstein-Barr virus (HHV-4)

Infectious mononucleosis

- Infectious mononucleosis (glandular fever)
- Caused by the Epstein-Barr virus (also known as human herpes virus 4, HHV-4).
- It is most common in adolescents and young adults.

Features:

- 1) sore throat
- 2) **palatal petechiae**
- 3) pyrexia, malaise, anorexia, headache
- 4) lymphadenopathy
- 5) splenomegaly:
 - ⇒ occurs in around 50% of patients and
 - ⇒ may rarely predispose to **splenic rupture**
- 6) hepatitis
- 7) presence of 50% lymphocytes with at least **10% atypical lymphocytes**
- 8) haemolytic anaemia secondary to **cold agglutins** (IgM)
- 9) a maculopapular, pruritic rash:
 - ⇒ develops in around 99% of patients who take ampicillin/amoxicillin whilst they have infectious mononucleosis

Diagnosis:

- heterophil antibody test (**Monospot test**)

Management is supportive and includes:

- 1) rest during the early stages, drink plenty of fluid, avoid alcohol
- 2) simple analgesia for any aches or pains
- 3) consensus guidance in the UK is to avoid playing contact sports for **8 weeks** after having glandular fever to reduce the risk of **splenic rupture**

Epstein-Barr virus associated conditions

Malignancies associated with EBV infection

- 1) Burkitt's lymphoma*
- 2) Hodgkin's lymphoma
- 3) HIV-associated CNS lymphomas
- 4) Nasopharyngeal carcinoma (squamous cell cancer of the nasopharyngeal epithelium, is one of the most common cancers in southern China)

*EBV is currently thought to be associated with both African and sporadic Burkitt's

The non-malignant condition hairy leukoplakia is also associated with EBV infection with HIV CD4 count 200-500, unlike *Candida*, the lesions cannot be scraped off the tongue. responds to (HAART).

Cytomegalovirus (CMV)

Human herpes virus 5 (HHV-5)

- Cytomegalovirus (CMV) is one of the herpes viruses.
- It is thought that around 50% of people have been exposed to the CMV virus although it only usually causes disease in the immunocompromised, for example people with HIV or those on immunosuppressants following organ transplantation.

Pathophysiology:

- infected cells have an 'Owl's eye' appearance due to **intranuclear inclusion bodies**

Patterns of disease

A) Congenital CMV infection

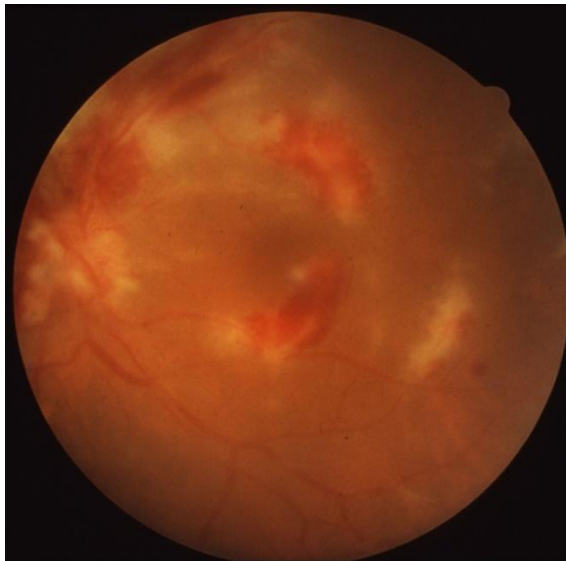
- features include:
 - 1) Growth retardation,
 - 2) Microcephaly, cp
 - 3) Pinpoint petechial 'blueberry muffin' skin lesions,
 - 4) Sensorineural deafness,
 - 5) Encephalitis (seizures)
 - 6) Hepatosplenomegaly, jaundice , anemia

B) CMV mononucleosis

- infectious mononucleosis-like illness
- may develop in immunocompetent individuals

C) CMV retinitis

- common in HIV patients with a low CD4 count (< 50)
- Presents with visual impairment e.g. 'blurred vision'.
- Fundoscopy shows retinal **haemorrhages** and **necrosis**, often called 'pizza' retina
- **IV ganciclovir** is the treatment of choice



D) CMV encephalopathy

- seen in patients with HIV who have low CD4 counts

E) CMV pneumonitis

F) CMV colitis

Kaposi's sarcoma

- The disease was originally described by Kaposi as a rare tumour in elderly men of Mediterranean origin ('classical Kaposi's sarcoma') in whom KS was usually found on the **lower legs** and **feet**.
- KS is now most commonly associated with **HIV disease** ('epidemic Kaposi's sarcoma'); it is seen predominantly in **gay men**.
- In **HIV** infection, KS lesions occur most commonly on the **face**; however lesions may be widely disseminated in **skin**, **bronchial tree** and **GIT**.
- KS can occur at any time during the course of HIV disease, **irrespective of CD4 count**; disseminated disease is commoner in late stage HIV disease/AIDS.
- It can also occur in elderly men without HIV
- It is induced by **human herpes virus 8** infection in patients with HIV
- Pulmonary disease:
 - ☒ Can present with dyspnoea and cough with **haemoptysis**;
 - ☒ It is usually associated with cutaneous disease, but can present in isolation.
 - ☒ Chest x ray may show **pulmonary nodules**.
- Kaposi's is on the decline due to the advent of highly active antiretroviral therapy.
- It most commonly presents on the lower limbs and patients may present with multiple lesions.
- It is considered a low-grade vascular malignancy.
- **TTT: radiotherapy + resection**



The picture shows characteristic purple lesions of Kaposi's sarcoma (KS) on the hard palate.



Kaposi's sarcoma (KS) of the eye.

Genital warts **النفرة** **(HPV 6&11)**

- also known as **condylomata accuminata**
- A common cause of attendance at genitourinary clinics.
- They are caused by the many varieties of the **human papilloma virus** HPV, especially types 6 & 11.

Features:

- 1) small (2 - 5 mm) fleshy protuberances which are slightly pigmented
- 2) may bleed or itch



Fig. 23.5 Viral wart.

Management:

- 1) **Topical podophyllum** or **cryotherapy** is commonly used as **first-line treatments** depending on the location and type of lesion:
 - ☒ **Multiple, non-keratinised warts** are generally best treated with **topical agents**
 - ☒ **Solitary, keratinised warts** respond better to **cryotherapy**
 - 2) **imiquimod** is a **topical cream** which is generally used **second line**
- ☒ **genital warts** are often resistant to treatment and recurrence is common although the majority of anogenital infections with HPV clear without intervention within 1-2 years

It is now well established that HPV (primarily types 16, 18 & 33) predisposes to cervical cancer.

Cervical dyskaryosis

- Although there are many potential causes for **irregular menstruation**, abnormal **bleeding** can be a sign of cervical dyskaryosis.
- Advanced HIV with **HPV** co-infection is a very strong risk factor for developing cervical dyskaryosis
- Currently the British HIV association recommend that patients with HIV should have **yearly smears**.
- The US guidelines recommend that HIV positive females under the age of 26 and MSM **should be immunised** as the HPV vaccine is safe and immunogenic at all CD4 counts.
- The risk of HPV infection already present is too great in patients older than 26 for cost effectiveness.
- British HIV guidelines on the use of the HPV vaccine in people living with HIV are currently awaited. In Britain the national programme now **immunises all females aged 12-13 years**.
- If cervical dyskaryosis is detected it is treated in the same way as in HIV negative patients.
- Cervical dyskaryosis is invisible to the naked eye and so a normal speculum examination does not rule out cervical disease.

H1N1 influenza pandemic

وباء انفلونزا الخنازير

- The 2009 H1N1 influenza (swine flu) outbreak was first observed in Mexico in early 2009.
- In June 2009, the WHO declared the outbreak to be a pandemic.

H1N1:

- The H1N1 virus is a subtype of the influenza A virus and the most common cause of flu in humans.
- The 2009 pandemic was caused by a new strain of the H1N1 virus.

The following groups are particularly at risk:

- 1) Patients with chronic illnesses and those on immunosuppressants
- 2) Pregnant women
- 3) Young children under 5 years old

Features:

The majority of symptoms are typical of those seen in a flu-like illness:

- 1) Fever greater than 38C
- 2) Myalgia
- 3) Lethargy
- 4) Headache
- 5) Rhinitis
- 6) Sore throat
- 7) Cough
- 8) Diarrhoea and vomiting

A minority of patients may go on to develop an acute respiratory distress syndrome **ARDS** which may require **ventilatory** support.

Treatment:

There are two main treatments currently available:

A) Oseltamivir (Tamiflu):

- 1) oral medication
- 2) **a neuraminidase inhibitor** which prevents new viral particles from being released by infected cells
- 3) common side-effects include:
 - 1) nausea, vomiting, diarrhoea
 - 2) headaches

oseltamivir 150 mg bd for ten days is the recommended treatment.

B) Zanamivir (Relenza):

- 1) inhaled medication
- 2) intravenous preparations are available for patients who are acutely unwell
- 3) also **a neuraminidase inhibitor**
- 4) may induce bronchospasm in asthmatics

For hospitalized influenza patients with suspected or known gastric stasis, gastric malabsorption, gastrointestinal bleeding, or for patients suspected or confirmed with oseltamivir-resistant influenza virus infection, intravenous zanamivir should be considered.

Zanamivir 300 mg IV for 10 days

Measles

الحصبة

- RNA paramyxovirus
- spread by droplets
- infective from prodrome until 4 days after rash starts
- incubation period = 10-14 days

Features:

- 1) prodrome: irritable, **conjunctivitis**, fever
- 2) **Koplik spots** (before rash): white spots ('grain of salt') on buccal mucosa
- 3) **rash**: starts behind ears then to whole body, discrete maculopapular rash becoming blotchy & confluent



Koplik spots -
body

The rash typically starts behind the ears and then spreads to the whole

Complications:

- 1) **encephalitis**: typically occurs 1-2 weeks following the onset of the illness
- 2) **subacute sclerosing panencephalitis** SSPE very rare, may present 5-10 years following illness
- 3) **febrile convulsions**
- 4) **giant cell pneumonia**
- 5) **keratoconjunctivitis**, corneal ulceration
- 6) diarrhoea
- 7) increased incidence of **appendicitis**
- 8) **myocarditis**

Management of contacts

If a child not immunized against measles comes into contact with measles:

⇒ **MMR should be offered**

(Vaccine-induced measles antibody develops more rapidly than that following natural infection)

⇒ this should be given **within 72 hours**

Rubella

الحصبة الألمانية

- Rubella is characterized by a **maculopapular nonconfluent rash** that is **pink**; it is often associated with **suboccipital lymphadenopathy** and **arthralgia**.
- The rash associated with measles is typically **red**, and **less frequently** associated with lymphadenopathy
- A **positive** rubella haemagglutination inhibition (HAI) combined with a **negative** rubella IgM is consistent with:
 - 1) Early acute infection with rubella
 - 2) Previous vaccination, or
 - 3) Previous rubella infection.

The most important issue to resolve is whether she has acute rubella.

The IgM may take several days to rise and the test should be repeated one to two weeks later.

Parvovirus B19

(erythrogenic virus)

- A single-strand DNA virus which causes a variety of clinical presentations
- It was identified in the 1980's as the cause of **erythema infectiosum**

Erythema infectiosum: (also known as fifth disease or 'slapped-cheek syndrome')

- most common presenting illness
- systemic symptoms: lethargy, fever, headache
- 'slapped-cheek' rash:
 - ⇒ both cheeks appear bright red as though they had been slapped
 - ⇒ spreading to proximal arms and extensor surfaces

Other presentations

- 1) asymptomatic
 - 2) pancytopenia in immunosuppressed patients
 - 3) symmetrical post-infectious arthritis
 - 4) aplastic crises e.g. in sickle-cell disease
 - ⇒ Parvovirus B19 suppresses erythropoiesis for about a week
 - ⇒ so aplastic anaemia is rare unless there is a chronic haemolytic anaemia
- The virus has a tropism for rapidly dividing erythrocyte precursors which they infect and destroy. Thus, no reticulocytes (immature erythrocytes) are available to replace aging or damaged erythrocytes as they are cleared by the reticuloendothelial system.
 - This may not have any significant impact on otherwise healthy individuals, but can trigger an aplastic crisis - particularly in patients with haemoglobinopathies.

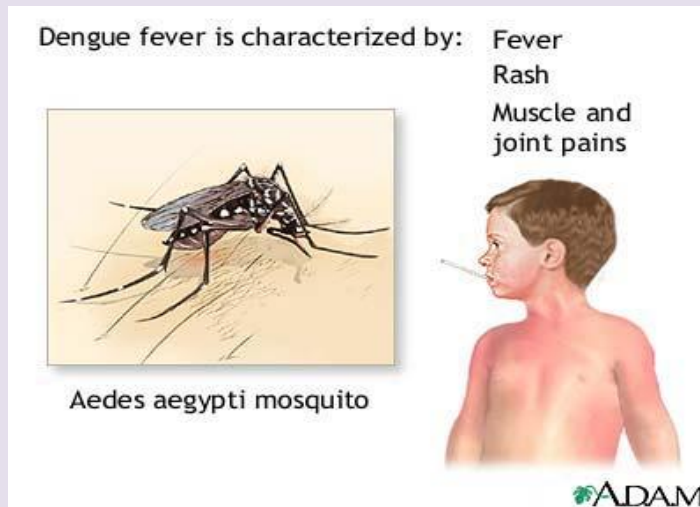
Symmetrical post-infectious arthritis

- Parvovirus B19 infection may also be associated with a symmetrical post-infectious arthritis,
- Affecting the small joints of the hands and feet.
- The knees or elbows are rarely involved.
- The arthritis is much more common in adults, particularly in women, and may persist for weeks to months (even years).
- The arthritis may mimic rheumatoid arthritis.
- Unlike rheumatoid arthritis, it does not cause permanent damage to bones or joints.

Dengue fever

حمى الضنك

- Dengue fever is a viral infection which can progress to **viral haemorrhagic fever**
- also yellow fever, Lassa fever, Ebola
- transmitted by the **Aedes aegypti mosquito**
- incubation period of **7 days**
- a form of disseminated intravascular coagulation (DIC) known as **dengue haemorrhagic fever** (DHF) may develop
- Around 20-30% of these patients go on to develop **dengue shock syndrome** (DSS)



Features:

- 1) Headache (often **retro-orbital**) مهمة جدا
- 2) Facial flushing (dengue)
- 3) Fever
- 4) There is often adenopathy, **palatal vesicles** and **sclera injection** on the first day
- 5) Myalgia
- 6) Pleuritic pain
- 7) **Maculopapular rash**

Treatment: is entirely **symptomatic** e.g. fluid resuscitation, blood transfusion etc

NB: Infectious mononucleosis cause palatal petechiae)

N.B. The yellow fever mosquito (Aedes aegypti) is a **mosquito** that can spread **dengue fever**, **chikungunya**, and **yellow fever** viruses, and other diseases. The mosquito originated in Africa,^[2] but is now found in **tropical** and subtropical regions throughout the world

A 40-year-old company executive went to Mexico for a four day business trip. Five days after her return to the United Kingdom she is said to have got a fever, headache, pains at the back of the eyes, back pain and severe muscle pain. She reports development of a rash of late which started on the trunk and spread to the extremities and the face. On examination she is ill-looking. Her temperature is 38°C and BP 120/70 mmHg. She has a scleral injection. Her adenoids are swollen with palatal vesicles. The patient has a maculopapular rash all over her body. Most likely diagnosis is dengue fever

West Nile encephalitis

- Caused by **Flavivirus**
- **May present with:**
 - 1) **Seizures**,
 - 2) reduced level of **consciousness**,
 - 3) a flaccid **paralysis** resembling poliomyelitis and
 - 4) **parkinsonian movement** disorders.
- Or
- 5) **Subtle convulsive status**, the only manifestation of which may be the **twitching** of a digit or a muscle group,
- May be associated with a grave prognosis in **Flavivirus** encephalitis or meningitis.
- The travel history adds weight to the diagnosis.

Diagnosis:

- 1) **The MRI** show high signal intensity and swelling in the **thalamus bilaterally**.
- 2) **Real-time polymerase chain reaction (PCR)** of cerebrospinal fluid (CSF) may identify viral RNA.

Management:

- **Interferon-alpha** has been the only treatment which may affect outcome in the treatment of West Nile encephalitis.
- =====

Rabies داء الكلب

- Rabies is a viral disease that causes **acute encephalitis**.
- The rabies virus is classed as a **RNA rhabdovirus** and has a bullet shaped capsid.
- It is commonly transmitted by bat الخفاش, raccoon and skunk الظربان الأمريكي bites.
- Following a bite the virus travels up the nerve axons towards the CNS in a retrograde fashion.

Features:

- 1) prodrome: headache, fever, agitation
- 2) hydrophobia: water-provoking muscle spasms
- 3) hypersalivation
- 4) Negri bodies: cytoplasmic inclusion bodies found in infected neurons

There is now considered to be 'no risk' of developing rabies following an animal bite in the UK and the majority of developed countries.

Following an animal bite in at risk countries:

- 1) if an individual is **already immunised**:
 - ⇒ **2 further doses** of vaccine should be given
- 2) if **not previously immunised** then
 - ⇒ **human rabies immunoglobulin (HRIG)** should be given along with;
 - ⇒ **a full course of vaccination**

Post-exposure prophylaxis

Hepatitis A

- ⇒ Human Normal Immunoglobulin (HNIG)
- Or
- ⇒ hepatitis A vaccine may be used depending on the clinical situation

Hepatitis B

1) HBsAg positive source:

- ☒ If the person exposed is a **known responder to HBV vaccine** then;
 - ⇒ **a booster dose** should be given
- ☒ If they are **in the process of being vaccinated** or are a **non-responder** then;
 - ⇒ **hepatitis B immune globulin (HBIG)** and
 - ⇒ **the vaccine** should be given

2) unknown source:

- ☒ for known responders the green book advises considering **a booster dose** of HBV vaccine
- ☒ For known non-responders **HBIG + vaccine** should be given
- ☒ whilst those in the process of being vaccinated should have an **accelerated course of HBV vaccine**

Hepatitis C

- monthly PCR ⇒ if seroconversion then ⇒ interferon +/- ribavirin

HIV:

- 1) **A combination of oral antiretrovirals** (e.g. Tenofovir, emtricitabine, lopinavir and ritonavir) ...ASAP... (i.e. Within 1-2 hours, but may be started up to 72 hours following exposure) for 4 weeks
- 2) serological testing at 12 weeks following completion of post-exposure prophylaxis
- 3) reduces risk of transmission by 80%

Varicella zoster:

- **VZIG** for IgG negative pregnant women/immunosuppressed

Estimates of transmission risk for single needle stick injury

Hepatitis B	20-30%
Hepatitis C	0.5-2%
HIV	0.3%

HIV and pregnancy

- With the increased incidence of HIV infection amongst the heterosexual population there are an increasing number of HIV positive women giving birth in the UK.
- In London the incidence may be as high as **0.4% of pregnant women**.
- The aim of treating HIV positive women during pregnancy is to minimize harm to both the mother and fetus, and to reduce the chance of vertical transmission.
- Guidelines regularly change on this subject

Factors which reduce vertical transmission: (from 25-30% to----- 2%)

- 1) maternal antiretroviral therapy
- 2) mode of delivery (caesarean section)
- 3) neonatal antiretroviral therapy
- 4) infant feeding (bottle feeding)

Screening:

NICE guidelines recommend offering HIV screening to all pregnant women (also HBV & Smoking by CO)

Antiretroviral therapy:

- 1) all pregnant women should be offered antiretroviral therapy regardless of whether they were taking it previously
- 2) If women are not currently taking antiretroviral therapy
 - ⇒ The RCOG recommend that it is commenced between 28 and 32 weeks of gestation and should be continued intrapartum.
 - ⇒ BHIVA recommend that antiretroviral therapy may be started at an earlier gestation depending upon the individual situation

Mode of delivery

- vaginal delivery is recommenced if viral load is less than **50 copies/ml** at 36 weeks, otherwise caesarian section is recommended
- **a zidovudine infusion** should be started 4 hours before beginning the caesarean section

Neonatal antiretroviral therapy

- ⇒ Zidovudine is usually administered orally to the neonate if maternal viral load is <50 copies/ml.
- ⇒ Otherwise **triple ART** should be used.
- ⇒ Therapy should be continued for **4-6 weeks**.

Infant feeding

- in the UK all women should be advised **not to breast feed**

HIV: Cytomegalovirus retinitis

- CMV retinitis is common, affecting 30-40% of patients who have a CD4 count < 50
- Diagnosis is clinical as there are no diagnostic tests

Features:

- visual impairment - 'blurred vision' etc

Fundoscopy:

- characteristic appearance showing retinal hemorrhages and necrosis, often called 'pizza' retina (cottage cheese and tomato ketchup)

Management:

- 1) IV ganciclovir
- 2) treatment used to be **life-long** but new evidence suggests that it may be discontinued once CD4 > 150 after HAART
- 3) alternative: IV foscarnet or cidofovir

HIV: diarrhoea

- Diarrhoea is common in patients with HIV.
- This may be due to the effects of the virus itself (HIV enteritis) or opportunistic infections

Possible causes:

- 1) Cryptosporidium + other protozoa (most common)
- 2) CMV
- 3) Mycobacterium avium intracellulare
- 4) Giardia

Cryptosporidium

- The most common infective cause of diarrhoea in HIV patients.
 - It is an **intracellular protozoa**
 - Incubation period: **7 days**.
 - Presentation is very variable, ranging from mild to severe diarrhoea.
 - **A modified Ziehl-Neelsen stain** (acid-fast stain) of the stool may reveal the characteristic **red cysts of Cryptosporidium**.
 - Treatment is difficult, with the mainstay of management being supportive therapy*
- *nitazoxanide is licensed in the US for immunocompetent patients

Mycobacterium avium intracellulare

- An atypical mycobacteria seen with the CD4 count < 50
- Typical features include fever, sweats, abdominal pain & diarrhoea.
- There may be hepatomegaly and deranged LFTs.

Diagnosis by:

- 1) blood cultures and
- 2) Bone marrow examination.

Management is with:

- 1) rifabutin,
- 2) ethambutol and
- 3) clarithromycin

HIV: biliary and pancreatic disease

- 1) The most common cause of biliary disease in patients with HIV is **sclerosing cholangitis** due to infections such as **CMV**, **Cryptosporidium** and **Microsporidia**
- 2) Pancreatitis in the context of HIV infection may be secondary to:
 - 1) anti-retroviral treatment (especially **didanosine**) or by
 - 2) opportunistic infections e.g. **CMV**

HIV: oesophageal candidiasis

- Oesophageal candidiasis is the most common cause of oesophagitis in patients with HIV.
- It is generally seen in patients with a CD4 count < 100.
- Typical symptoms include dysphagia and odynophagia.
- Oral or IV **Fluconazole** and **itraconazole** are first-line treatments (2-3 weeks)
- Although **oropharyngeal candidiasis** may be treated with topical antifungal agents (such as nystatin, clotrimazole, and amphotericin B oral suspension/lozenges) Candida oesophagitis requires oral or IV therapy (usually with fluconazole or itraconazole for at least 14-21 days).
- Topical therapy is inadequate.

HIV: Kaposi's sarcoma

- caused by HHV-8 (human herpes virus 8)
- presents as purple papules or plaques on the skin or mucosa (e.g. gastrointestinal and respiratory tract)
- skin lesions may later ulcerate
- respiratory involvement may cause massive haemoptysis and pleural effusion
- **radiotherapy + resection**

HIV immunisation

The Department of Health 'Greenbook' on immunisation defers to the British HIV Association for guidelines relating to immunisation of HIV-infected adults

Vaccines that can be used in all HIV-infected adults	Vaccines that can be used if CD4 > 200	Contraindicated in HIV-infected adults
• Hepatitis A & B • Rabies, Japanese encephalitis • Influenza-parenteral • Poliomyelitis-parenteral (IPV) • Haemophilus influenzae B (Hib) • Meningococcus-MenC • Meningococcus-ACWY I • Pneumococcus-PPV23 • Tetanus-Diphtheria (Td)	• MMR • Varicella • Yellow Fever	• Cholera CVD103-HgR • Tuberculosis (BCG) • Influenza-intranasal • Poliomyelitis-oral (OPV)

HIV seroconversion

- HIV seroconversion is symptomatic in 60-80% of patients and
- typically presents as a glandular fever type illness
- Increased symptomatic severity is associated with poorer long term prognosis.
- It typically occurs **3 weeks - 3 months** after infection

Features:

- 1) sore throat (severe pharyngitis)
- 2) mouth ulcers
- 3) lymphadenopathy
- 4) malaise, myalgia, arthralgia
- 5) diarrhoea
- 6) maculopapular rash
- 7) rarely meningoencephalitis

Diagnosis:

- antibodies to HIV may not be present
- **HIV PCR** and **p24 antigen** tests can confirm diagnosis

EBV, CMV & acute HIV التلاثة ممكن يعملوا ----> **Glandular fever**
(Infectious mononucleosis like illness)
Toxoplasma هي كمان تعمل زيهم.

HIV Neurocomplications

Focal neurological lesions

Toxoplasmosis

- accounts for around 50% of cerebral lesions in patients with HIV
- constitutional symptoms, headache, confusion, drowsiness

CT:

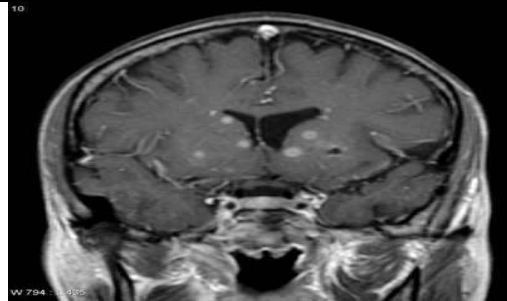
- 1) usually **single** or **multiple** ring enhancing lesions,
- 2) mass effect may be seen

Management:

- 1) **Sulfadiazine** and
- 2) **Pyrimethamine**



Cerebral toxoplasmosis: CT scan with contrast showing multiple ring enhancing lesions



Cerebral toxoplasmosis: MRI (T1 C+) demonstrates multiple small peripherally enhancing nodules located predominantly in the basal ganglia as well as the central portions of the cerebellar hemispheres. Only a small amount of surrounding oedema is present.

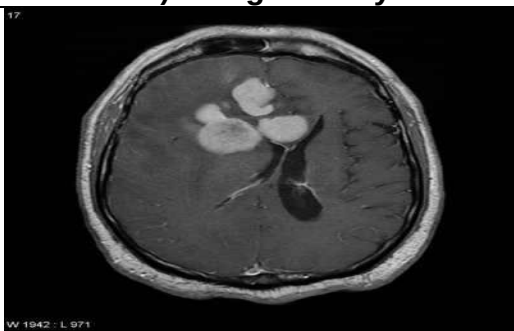
Primary CNS lymphoma

- accounts for around 30% of cerebral lesions
- associated with the **Epstein-Barr virus**

CT: single or multiple **homogenous enhancing lesions**

Treatment:

- 1) Generally involves **steroids** (may significantly reduce tumour size),
- 2) Chemotherapy (e.g. **methotrexate**) + with or without whole **brain irradiation**.
- 3) Surgical may be considered for lower grade tumours



A) Primary CNS lymphoma: MRI (T1 C+) demonstrates a large multilobulated mass in the right frontal lobe. It homogeneously enhances and extends to involve the caudate and the periventricular area. There is significant mass effect.



B) Primary CNS lymphoma: Non-contrast CT demonstrates a hyper-attenuating mass adjacent to the left lateral ventricle, with no calcification or haemorrhage.

Differentiating between toxoplasmosis and lymphoma

Toxoplasmosis	Lymphoma SSS
• Multiple lesions • Ring or nodular enhancement • Thallium SPECT negative	• Single lesion • Solid (homogenous) enhancement • Thallium SPECT positive

Tuberculosis

- much less common than toxoplasmosis or primary CNS lymphoma
- CT: **single enhancing lesion**

Generalised HIV neurocomplications

Encephalitis

- may be due to CMV or HIV itself
- HSV encephalitis but is relatively rare in the context of HIV
- CT: **oedematous brain**

Cryptococcus neoformans

- **Most common fungal infection of CNS**, CD4 < 50 cells/mm³ and
- May be associated with a pneumonitis.
- Cryptococcus can cause **papular skin lesions** that **resemble molluscum contagiosum**.
- The disease is commoner in **African populations**.

Features:

- 1) **Meningitis** is typical presentation but may occasionally cause a **space occupying lesion**
- 2) headache, fever, malaise,
- 3) nausea/vomiting,
- 4) seizures, focal neurological deficit
- **CSF:**
 - 1) high opening pressure,
 - 2) **India ink test positive thick polysaccharide capsule** around the cell
- **CT:**
 - 1) **meningeal enhancement**,
 - 2) cerebral oedema

Treatment:

- 1) **Amphotericin B** and **flucytosine (5FC)**;
- 2) Patients then require lifetime suppression with **fluconazole**.



India ink stain shows: the thick polysaccharide capsule is highlighted around the cell (shown in slide).

Progressive multifocal leukoencephalopathy (PML)

- Widespread demyelination
- due to infection of oligodendrocytes by JC virus (a polyoma DNA virus)
- symptoms; subacute onset of;
 - 1) behavioral changes,
 - 2) speech, motor, visual impairment
- **CT:**
 - 1) Single or multiple lesions,
 - 2) no mass effect,
 - 3) Don't usually enhance.
- **MRI:**
 - ✓ Better
 - ✓ high-signal demyelinating white matter lesions are seen

AIDS dementia complex

- caused by HIV virus itself
- **Symptoms:**
 - ✓ behavioral changes,
 - ✓ motor impairment
- **CT:** cortical and subcortical atrophy

Eosinophilic folliculitis (EF)

- A common pruritic dermatosis, often associated with HIV disease.
- **There are three main variants of EF:**
 - 1) **Classic EF**
 - 2) Immunosuppression-related EF (mostly HIV-associated) and
 - 3) Infancy-associated EF.

Classic EF:

- Also known as Ofuji disease (eosinophilic pustular folliculitis),
- More common in individuals of Japanese descent, although anyone can be affected.
- The clinical presentations of EF vary slightly, but histologically the forms are identical.

Immunosuppression-related (HIV-associated):

- The most common type of EF
- It differs from the classical form in that the eruption is exquisitely **pruritic**.
- It also tends to present with erythematous, almost oedematous, **papules** with **few pustules**
(Whereas the classic form tends to have clusters of pustules)
- Because the eruption is so pruritic the lesions are often **excoriated** on presentation, making identification of a primary lesion difficult.
- The lesions are found primarily on **the face** and **upper trunk** (from the waist up).
- **Men** seem to be more commonly affected than women.
- The patient's **CD4+ cell count** is often **below 250/μL**
- Patients may have a **peripheral eosinophilia** and **lymphopenia**.
- Cases may worsen **three months** to **six months** after the initiation of antiretroviral therapy as part of the immune restoration syndrome and even after the CD4+ cell count rises above 200/μL.
- The reason for this development is unknown, but may represent a previously quiescent immune system now reacting to antigens.
- **Histologic examination** of a papule shows:
 - 1) an acute and chronic infiltrate of eosinophils and lymphocytes
 - 2) Focused at the level of the follicular isthmus that can rarely progress to complete follicular destruction.

Differential Diagnosis

- **Acne vulgaris** may look similar to EF, but EF is highly pruritic, whereas acne is not. This symptom alone can be helpful in differentiating the two disease processes.
- Acne may also present with comedones, which are not observed in this patient.
- Involvement of the postauricular scalp is also not typical of acne vulgaris (chloracne is the exception and originates from exposure to chlorinated aromatic hydrocarbons).

- **Rosacea** can present with varying manifestations such as flushing, non-pruritic papules, rhinophymatous changes, telangiectasias on the face, and even with ocular involvement such as a "gritty" sensation. Although papules are seen on this patient, none of the other sequelae of rosacea are found, excluding this condition.
- Despite **drug eruptions** being common in HIV-infected patients, a drug eruption would typically have a more diffuse presentation, whereas EF typically involves the skin from the waist up. A biopsy would aid in the diagnosis if a drug eruption were a consideration.
- **Papular urticaria** is manifested by chronic or recurrent papules caused by hypersensitivity reactions to bites of mosquitoes, fleas, bedbugs and other insects. Individual papules may surround a wheal or display a central punctum.
- The eruption is characterised by crops of symmetrically distributed pruritic papules and papulovesicles which appear in an area localised to the site of insect bites but they occur in any part of the body.
- The lesions tend to be on exposed areas particularly extensor surfaces of the extremities.

Orf

- Orf is generally a condition found in sheep and goats although it can be transmitted to humans.
- It is caused by the parapox virus.

In animals:

- 'scabby' lesions around the mouth and nose

In humans:

- 1) generally affects the hands and arms
- 2) initially small, raised, red-blue papules
- 3) later may increase in size to 2-3 cm and become flat-topped and haemorrhagic

Antiviral agents

Drug	Mechanism of action	Indications	Adverse effects/toxicity
Aciclovir	- Guanosine analog, - phosphorylated by thymidine kinase which in turn inhibits the viral DNA polymerase	HSV, VZV	Crystalline nephropathy
Ganciclovir		CMV	Myelosuppression/ agranulocytosis
Cidofovir	Acyclic nucleoside phosphonate, so independent of phosphorylation by viral enzymes (compare aciclovir/ ganciclovir) inhibit viral DNA polymerase	CMV retinitis in HIV	Nephrotoxicity
Foscarnet	Pyrophosphate analog which inhibits viral DNA polymerase	CMV, HSV if not responding to acyclovir	Nephrotoxicity, hypocalcaemia, hypomagnesaemia, seizures
Amantadine	- Inhibits uncoating (M2 protein) of virus in cell. - Also releases dopamine from nerve endings	Influenza, Parkinson's disease	Confusion, ataxia, slurred speech
Oseltamivir	Inhibits neuraminidase	Influenza	Headache, GIT upset
Interferon-α	- Human glycoprotein - which inhibit synthesis of mRNA	Chronic hepatitis B & C, hairy cell leukaemia	Flu-like symptoms, anorexia, myelosuppression
Ribavirin (R—RNA)	- Guanosine analog - inhibits inosine monophosphate (IMP) dehydrogenase, - interferes with the capping of viral mRNA	Chronic HCV, RSV	Haemolytic anaemia

Anti-retroviral agent used in HIV should be started once CD4 <350

- 1) **Nucleoside analogue reverse transcriptase inhibitors (NRTI)**
 - examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine
- 2) **Non-nucleoside reverse transcriptase inhibitors (NNRTI)**
 - examples: nevirapine, efavirenz
- 3) **Protease inhibitors (PI)**
 - inhibits a protease needed to make the virus able to survive outside the cell
 - examples: indinavir, nelfinavir, ritonavir, saquinavir

Protozoa

Leishmaniasis

- Leishmaniasis is caused by the **intracellular** protozoa *Leishmania*,
- usually being spread by **sand flies**
- **3 types:**

A) **Cutaneous leishmaniasis:**

- ☒ caused by *Leishmania tropica* or *Leishmania mexicana*
- ☒ **crusted lesion** at site of bite
- ☒ may be underlying **ulcer**

B) **Mucocutaneous leishmaniasis:**

- ☒ caused by *Leishmania braziliensis*
- ☒ skin lesions may spread to involve **mucosae of nose, pharynx** etc

C) **Visceral leishmaniasis (kala-azar)**

- ☒ mostly caused by *Leishmania donovani*
- ☒ occurs in the **Mediterranean, Asia, South America, Africa**

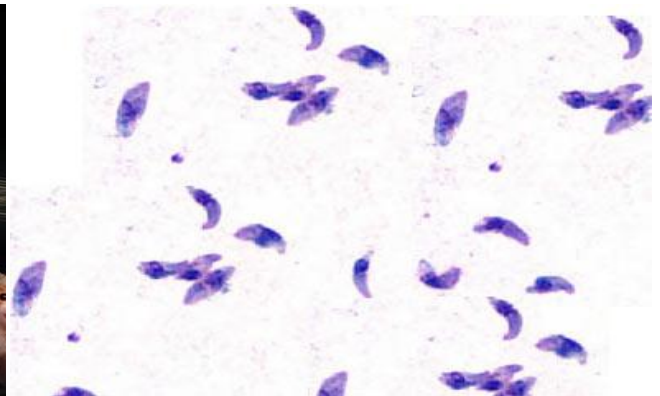
Features:

- 1) fever, sweats, rigors
- 2) Massive splenomegaly & hepatomegaly
- 3) poor appetite*, weight loss
- 4) grey skin - '**kala-azar**' means black sickness
- 5) pancytopenia secondary to **hypersplenism**

*occasionally patients may report increased appetite with paradoxical weight loss

Protozoa

Toxoplasmosis



- **Toxoplasma gondii** is a protozoa which infects the body via the GIT, lung or broken skin
- Its **oocysts** release **trophozoites** which **migrate** widely around the body including to the eye, brain and muscle.
- The usual animal reservoir is the **cat**, although other animals as **rats** carry the disease
- Most infections are asymptomatic.
- Symptomatic patients usually have a self-limiting infection, often having clinical features **resembling infectious mononucleosis** (fever, malaise, lymphadenopathy)
- Other less common manifestations include **meningoencephalitis** and **myocarditis**.

Investigation:

- antibody test
- Sabin-Feldman dye test

Treatment:

- ☒ usually reserved for those with severe infections or patients who are immunosuppressed
- ☒ **pyrimethamine** plus **sulphadiazine** for at least 6 weeks

Congenital toxoplasmosis

- is due to transplacental spread from the mother
- **It causes a variety of effects to the unborn child including:**
 - 1) microcephaly,
 - 2) hydrocephalus,
 - 3) cerebral calcification and
 - 4) choroidoretinitis
 - 5) cerebral palsy &
 - 6) hepatomegaly

Toxoplasmosis congénita



Protozoa

Trypanosomiasis

- **Two main form of this protozoal disease are recognized:**

- 1) African trypanosomiasis (**sleeping sickness**) and
- 2) American trypanosomiasis (**Chagas' disease**)

African trypanosomiasis

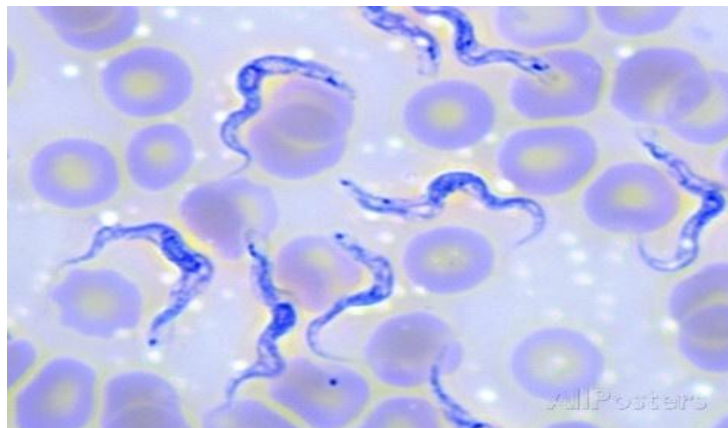
- Two forms of African trypanosomiasis, or **sleeping sickness**, are seen:
 - 1) Trypanosoma **gambiense** in West Africa and
 - 2) Trypanosoma **rhodesiense** in East Africa.
- Both types are spread by the **tsetse fly**.
- Trypanosoma rhodesiense tends to follow a **more acute** course (death within weeks or months, rash > Lymphadenopathy).

Clinical features include:

- 1) Trypanosoma chancre - painless subcutaneous nodule at site of infection
- 2) **intermittent fever**
- 3) enlargement of **posterior cervical lymph nodes**
- 4) A **rash** sometimes occurs and mild **hepatosplenomegaly** may develop.
- 5) Later:---> **CNS involvement** e.g. somnolence, headaches, mood changes, meningoencephalitis Extrapyrimal signs and ataxia are common

Management:

- 1) early disease:
 - ⇒ **IV pentamidine** or
 - ⇒ **suramin**
- 2) later disease or CNS involvement:
 - ☒ **IV melarsoprol**



Trypanosoma Gambiensi

American trypanosomiasis (Chagas' disease)

- Caused by the protozoan *Trypanosoma cruzi* which infects humans via a blood sucking insect vector (*triatomine bugs*).



Acute phase:

- The vast majority of patients (95%) are asymptomatic in the acute phase
- A **chagoma** (an erythematous nodule at site of infection) and **periorbital oedema** are sometimes seen.



Chronic Chagas' disease mainly affects the heart and GIT

1) Myocarditis:

- ☒ may lead to heart failure and arrhythmias
- ☒ Cardiac involvement is the leading cause of death in Chagas disease

2) gastrointestinal features includes:

- ☒ megaoesophagus causing dysphagia
- ☒ megacolon causing constipation

Management:

- 1) treatment is most effective in the acute phase using azole or nitro-derivatives such as **benznidazole** or **nifurtimox**
- 2) chronic disease management involves treating the complications e.g., heart failure



Chagas mega-esophagus

Filarial infection

- Filariasis (or philariasis) is a parasitic disease caused by an infection with roundworms of the Filarioidea type.
 - These are spread by **blood-feeding black flies** and **mosquitoes**.
 - This disease belongs to the group of diseases called helminthiasis.
 - 8 known filarial nematodes use humans as their definitive hosts. These are divided into 3 groups according to the niche مكان within the body they occupy:
- 1) **Lymphatic filariasis:**
 - Caused by the worms **Wuchereria bancrofti**, **Brugia malayi**, and **Brugia timori**.
 - These worms occupy the lymphatic system, including the lymph nodes; in chronic cases, these worms lead to the disease elephantiasis.
 - 2) **Subcutaneous filariasis:**
 - Caused by **Loa loa** (the eye worm), **Mansonella streptocerca**, and **Onchocerca volvulus**.
 - These worms occupy the subcutaneous layer of the skin, in the fat layer.
 - L. loa causes Loa loa filariasis, while O. volvulus causes **river blindness**.
 - 3) **Serous cavity filariasis:**
 - Caused by the worms **Mansonella perstans** and **Mansonella ozzardi**, which occupy the serous cavity of the abdomen.

Onchocerciasis:

- Also known as **river blindness** and **Robles disease**,
- a disease caused by infection with the parasitic worm **Onchocerca volvulus**
- Symptoms include severe itching, bumps under the skin, and blindness.
- It is the second most common cause of **blindness due to infection**, after trachoma.

Loiasis

- Loiasis is a filarial infection caused by *Loa Loa*.
- It is transmitted by the *Chrysops deerfly* (yellow flies)ذباب الغزلان.....الدبان الاصفر...
- Occur in rainforest regions of Western and Central Africa... غرب ووسط افريقيا... الغابات المطيرة...

Clinical features:

- 1) pruritus
 - 2) urticaria
 - 3) Calabar swellings: transient, non-erythematous, hot swelling of soft-tissue around joints
 - 4) 'Eye worm' the dramatic presentation of subconjunctival migration of the adult worm.
(African eye worm)
 - 5) It has less pathological features than other the microfilarial infections Onchocerciasis and Lymphatic Filariasis.
 - 6) However high loa loa microfilaraemia is associated with **encephalopathy** following treatment with either **Ivermectin** or DEC (**diethylcarbamazine**).
 - ⇒ This occurs due to the death of vast numbers of blood microfilaria.
 - ⇒ Both of these drugs are contraindicated if loa loa microfilaraemia exceeds 2500 mf/ml.
- This has significant public health implications as **Ivermectin** is currently the drug of choice for control of both Onchocerciasis and Lymphatic Filariasis in Africa.

Tropical eosinophilia

- An allergic reaction to microfilaria of *Wuchereria bancrofti*.
- **Characteristic features include:**
 - 1) myalgia; fatigue; weight loss;
 - 2) cough and dyspnoea with wheeze;
 - 3) fever;
 - 4) current or previous residence in an area endemic for filariasis (southern Asia, Africa, India, South America);
 - 5) lymphadenopathy;
 - 6) Marked peripheral blood **eosinophilia** and **high titres of anti-filarial antibodies**.
- **The chest x ray** shows bilateral reticulonodular shadowing.
- This condition is commonly accompanied by false positive serological tests for syphilis and high titres of cold agglutinins.
- There is typically a rapid response to treatment with **diethylcarbamazine**.

Nematodes الدودة الخيطية

1) Ancylostoma braziliense

- Hookworms (الديدان الخطافية)
- most common cause of **cutaneous larva migrans**
- common in Central and Southern America
- The infection is acquired by direct contact with **dog or cat faeces** - often when sunbathing on contaminated sand.
- The larvae burrow in dermo-epidermal junction.
- Symptoms include pruritus and a raised, serpiginous erythematous rash that migrates at a rate of up to 1 cm/day.

Treatment:

- The disease is self-limiting but the duration of disease varies considerably.
- **Oral ivermectin** in a single dose of 200 µg/kg body weight is the main treatment.
- Other treatment options include **oral albendazole** or **topical thiabendazole**.



2) Strongyloides stercoralis

- Infection with Strongyloides stercoralis causes strongyloidias
- Acquired percutaneously (e.g. **walking barefoot**).
- The larvae are present in **soil** and gain access to the body by penetrating the skin.
- **papulovesicular** lesions where the skin has been penetrated by infective larvae e.g. soles and buttocks.
- causes **pruritus** and **larva currens** (pruritic, linear, urticarial rash) this has a similar appearance to **cutaneous larva migrans** but moves through the skin at **a far greater rate**
- **abdo pain**, **diarrhoea**, **pneumonitis** (if the larvae migrate to the lungs a pneumonitis similar to Loeffler's syndrome may be triggered)
- may cause Gram negative septicaemia due carrying of bacteria into bloodstream
- **eosinophilia** sometimes seen

Management:

- 1) thiabendazole, albendazole.
- 2) Ivermectin also used, particularly in chronic infections.

3) **Toxocara canis (الكلب)**

- commonly acquired by ingesting eggs from soil contaminated by dog faeces
- commonest cause of **visceral larva migrans**
- other features: eye granulomas (**macular**), liver/lung involvement



The slide shows the typical appearance of *Toxocara* retinitis with a lesion at the macula. In retinitis due to *Toxocara canis*, there is usually only a single, well demarcated lesion.

4) **Ascaris lumbricoides**

- The most common nematode parasite of humans.
- A large roundworm, growing up to 35 cm in length
- Infected patients are often asymptomatic.
- Symptoms may develop as a result of;
 - ☒ pneumonitis caused by the worm's migration through the lungs,
 - ☒ obstruction of the gastrointestinal tract or
 - ☒ biliary/pancreatic duct obstruction
- **Piperazine** is the treatment of choice in patients presenting with bowel obstruction;
- **mebendazole** may be used to treat other infections.



Enterobius vermicularis الدبوسية (threadworm)

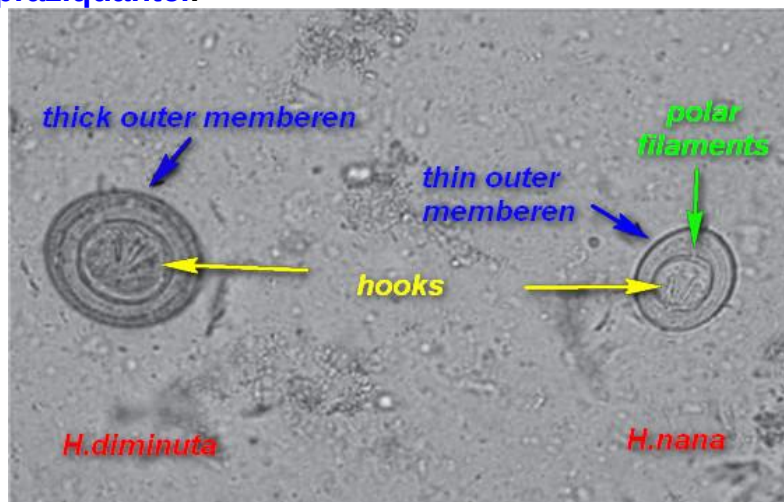
- Not uncommon in children and in institutions.
- Transmission is by the faeco-oral route
- Intense anal pruritus is the predominant symptom.
- Treatment is with **mebendazole**.



A perianal swab microscopy (*Enterobius vermicularis* egg)

Hymenolepis nana شريطية قزمة

- A rodent cestode parasite
- Can be transmitted to humans and usually affects children
- Abdominal pain, anorexia, diarrhoea, pruritus ani and urticaria are the most frequent symptoms.
- **Eosinophilia** may be present in heavy infestations.
- Treatment is with **praziquantel**.



Trichuriasis

- Commoner in malnourished populations;
- Symptoms are minimal but may result in growth retardation in children.
- Heavy burdens of infection may be associated with **bloody diarrhoea**;
- it is associated with rectal prolapse.
- Treatment is with **mebendazole**.

Tape worms

الديدان الشريطية

- Tape worms are made up of repeated segments called proglottids.
- These are often present in faeces and are useful diagnostically

Cysticercosis

- From asymptomatic to neurocysticercosis, seizures, and chronic meningitis
- **multiple enhancing unilocular cysts in brain**
- caused by:
 - ⇒ Taenia solium (from pork) and
 - ⇒ Taenia saginata (from beef)
- Management: **niclosamide**, **albendazole**

Hydatid disease

- Hydatid infection was endemic in sheep farming regions (such as Wales or New Zealand)
- Caused by the dog tapeworm: **Echinococcus granulosus**
- **Life-cycle involves:**
 - ☒ Dogs ingesting hydatid cysts from sheep liver.
 - ☒ Humans contract hydatids via faecal/oral spread from dogs.
- often seen in farmers
- may cause liver cysts
- **Asymptomatic, calcified** cystic lesions in the liver are typical of hydatid cysts.
- Calcification usually denotes a non-viable cyst.
- Ultrasonography is probably the most helpful initial test since it can usually differentiate a simple cyst from other cystic lesions. It should also be used for follow up.
- Hydatid serology has a sensitivity of 80-90%. If hydatid serology is negative then further imaging (CT/MRI) +/- aspiration may be required to make a diagnosis.

Management: **albendazole**

Schistosomiasis

- Schistosomiasis is one of the commonest protozoal infections.
- Schistosomiasis, or bilharzia, is a parasitic flatworm infection.
- **The following types of schistosomiasis are recognised:**
 - ☒ *Schistosoma mansoni* and *Schistosoma intercalatum*: **intestinal schistosomiasis**
 - ☒ *Schistosoma haematobium*: **urinary schistosomiasis**
 - ☒ *S. japonicum*: the commonest cause of ***Schistosoma* encephalitis**.

Schistosoma mansoni:

- Geographical distribution: Caribbean, eastern Mediterranean countries, South America, and most countries in Africa
- Causes: Intestinal schistosomiasis and liver disease (fibrosis, portal hypertension).
- Some patients with hepatosplenic disease develop schistosomal cor pulmonale.
- **Spinal schistosomiasis**, presenting as transverse myelitis ('traveller's myelitis'), is primarily due to *S. mansoni* infection.

Schistosoma haematobium:

- *S. haematobium* is prevalent and is found mainly in the Middle East, India, Portugal, Africa
- Causes: **Urinary tract disease**. Rarely causes intestinal or liver disease.
- This typically presents as a '**swimmer's itch**' in patients who have recently returned from Africa.
- *Schistosoma haematobium* is a risk factor for **squamous cell bladder cancer**

Features:

- 1) frequency
- 2) haematuria
- 3) bladder calcification

Management:

- single oral dose of praziquantel

Schistosoma japonicum:

- Geographical distribution: Western Pacific countries (China, Philippines, Indonesia, Thailand)
- It is the commonest cause of ***Schistosoma* encephalitis**.
- Its eggs are smaller unlike those of *S. masoni* and *S. haematobium*
- Causes: Intestinal schistosomiasis and liver disease (fibrosis, portal hypertension).

S. masoni and *S. haematobium* eggs are more likely to cause spinal cord schistosomiasis because of their larger size and spikes which do not enable them get to the brain hence the infection in the spinal cord.

- *S. mekongi* is found only in the Mekong river bed, that is in Laos and Cambodia in South East Asia.
- *S. intercalatum* is found in the forest areas of central and west Africa.

Management:

☒ Praziquantel:

- The treatment of choice for all *Schistosoma* species.
- Praziquantel is not licensed for human use in the United Kingdom but is available on named patient basis.

S. japonicum

- Praziquantel **60 mg/kg per day** for 6 days with a maximum dose of 5 grams per day with
- **prednisolone 1 mg/kg**.

S. mansoni and S. haematobium

- Praziquantel **40 mg/kg per day** for 3 days

☒ Since some of the pathology in neuroschistosomiasis is secondary to hypersensitivity reactions there is need to use a steroid, in this case **prednisolone 1 mg/kg per day**. There is no consensus about when it should be started or stopped.

☒ The symptoms of acute schistosomiasis are very similar to any acute viral or bacterial infection and it is therefore important to ESTABLISH a travel history to an endemic area.

☒ Some patients develop a rash at the site of entry of cercariae into the skin ('swimmer's itch') and others develop systemic upset (Katayama syndrome).

☒ Fever, lethargy, and myalgia are the most common symptoms; patients may also have cough, headache, anorexia, and a generalised rash.

☒ If acute schistosomiasis is unrecognised, chronic infection occurs.

☒ Presence of an **eosinophilia** - strongly suggestive of parasitic infection.

Vaccinations

It is important to be aware of vaccines which are of the live-attenuated type as these may pose a risk to immunocompromised patients. The main types of vaccine are as follows:

Live attenuated

- BCG
- measles, mumps, rubella (MMR)
- influenza (intranasal)
- oral polio
- yellow fever
- oral rotavirus
- oral typhoid (whole cell typhoid vaccine is no longer used in the UK)

Inactivated preparations

- rabies
- influenza (intramuscular)

Detoxified exotoxins

- tetanus

Extracts of the organism/virus (sometimes termed fragment)

May also be produced using recombinant DNA technology

- diphtheria
- pertussis ('acellular' vaccine)
- hepatitis B
- meningococcus, pneumococcus, haemophilus

Notes

- influenza: different types are available, including whole inactivated virus, split virion (virus particles disrupted by detergent treatment) and sub-unit (mainly haemagglutinin and neuraminidase)
- cholera: contains inactivated Inaba and Ogawa strains of *Vibrio cholerae* together with recombinant B-subunit of the cholera toxin
- hepatitis B: contains HBsAg adsorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology

Vaccines that can be used in all HIV-infected adults	Vaccines that can be used if CD4 > 200	Contraindicated in HIV-infected adults
Hepatitis A & B Rabies, Japanese encephalitis Influenza-parenteral Poliomyelitis-parenteral (IPV) Haemophilus influenzae B (Hib) Meningococcus-MenC Meningococcus-ACWY I Pneumococcus-PPV23 Tetanus-Diphtheria (Td)	MMR Varicella Yellow Fever	Cholera CVD103-HgR Tuberculosis (BCG) Influenza-intranasal Poliomyelitis-oral (OPV)

Pyrexia of unknown origin

Defined as a prolonged fever of > 3 weeks which resists diagnosis after a week in hospital

Neoplasia:

- 1) lymphoma
- 2) hypernephroma
- 3) preleukaemia
- 4) atrial myxoma

Infections:

- abscess
- TB

Connective tissue disorders

Splenectomy

Following a splenectomy patients are particularly at risk from pneumococcus, Haemophilus, meningococcus and Capnocytophaga canimorsus (usually from dog bites) infections

Vaccination

- if elective, should be done 2 weeks prior to operation
- Hib, meningitis A & C
- annual influenza vaccination
- pneumococcal vaccine every 5 years

Antibiotic prophylaxis

- **Penicillin V:**
 - ⇒ unfortunately clear guidelines do not exist of how long antibiotic prophylaxis should be continued
 - ⇒ It is generally accepted though that penicillin should be continued for at least 2 years and at least until the patient is 16 years of age,
 - ⇒ although the majority of patients are usually put on antibiotic prophylaxis for life

Lymphadenopathy

There are many causes of generalised lymphadenopathy

Infective:

- infectious mononucleosis
- HIV, including seroconversion illness
- toxoplasmosis
- CMV
- tuberculosis
- rubella
- roseola infantum
- eczema with secondary infection

Neoplastic:

- leukaemia
- lymphoma

Others:

- autoimmune conditions: SLE, rheumatoid arthritis
- graft versus host disease GVHR
- sarcoidosis
- drugs: phenytoin and to a lesser extent allopurinol, isoniazid

Vertebral infections

1) Tuberculosis:

- Common in intravenous drug users.
- Pott's disease affects the **thoracic** spine instead of the lumbar vertebrae which have the greatest blood supply.
- The other infections of the spine are usually found in the lumbar spine.

2) Brucella spine (brucellosis of the spine)

- The signs and symptoms will be very similar to Pott's disease, but the infection will often be in the **lumbar** region and not in the thoracic region.

3) Fungal osteomyelitis

- Like most of the other infections it will affect the **lumbar** spine.

4) Kaposi's sarcoma of the spine

- It is more likely to affect the vertebral spines and is more likely to affect the **lumbar** vertebrae.

5) Staphylococcus aureus spine infection

- The infection will show significant narrowing of the disc spaces and the infection will be in the **lumbar** region.

Antibiotic guidelines

The following is based on current BNF guidelines:

Respiratory system

Condition	Recommended treatment
Exacerbations of chronic bronchitis	Amoxicillin or tetracycline or clarithromycin
Uncomplicated community-acquired pneumonia	Amoxicillin (Doxycycline or clarithromycin in penicillin allergic, add flucloxacillin if staphylococci suspected e.g. In influenza)
Pneumonia possibly caused by atypical pathogens	Clarithromycin
Hospital-acquired pneumonia	Within 5 days of admission: co-amoxiclav or cefuroxime >5 days after admission: piperacillin with tazobactam OR a broad-spectrum cephalosporin (e.g. ceftazidime) OR a quinolone (e.g. ciprofloxacin)

Urinary tract

Condition	Recommended treatment
Lower urinary tract infection	Trimethoprim or nitrofurantoin. Alternative: amoxicillin or cephalosporin
Acute pyelonephritis	Broad-spectrum cephalosporin or quinolone
Acute prostatitis	Quinolone or trimethoprim

Skin

Condition	Recommended treatment
Impetigo	Topical fusidic acid, oral flucloxacillin or erythromycin if widespread
Cellulitis	Flucloxacillin (clarithromycin or clindomycin if penicillin-allergic)
Erysipelas	Phenoxymethylpenicillin (erythromycin if penicillin-allergic)
Animal or human bite	Co-amoxiclav (doxycycline + metronidazole if penicillin-allergic)
Mastitis during breast-feeding	Flucloxacillin

ENT

Condition	Recommended treatment
Throat infections	Phenoxymethylpenicillin (erythromycin alone if penicillin-allergic)
Sinusitis	Amoxicillin or doxycycline or erythromycin
Otitis media	Amoxicillin (erythromycin if penicillin-allergic)
Otitis externa*	Flucloxacillin (erythromycin if penicillin-allergic)
Periapical or periodontal abscess	Amoxicillin
Gingivitis: acute necrotising ulcerative	Metronidazole

Genital system

Condition	Recommended treatment
Gonorrhoea	Intramuscular ceftriaxone + oral azithromycin
Chlamydia	Doxycycline or azithromycin
Pelvic inflammatory disease	Oral ofloxacin + oral metronidazole or intramuscular ceftriaxone + oral doxycycline + oral metronidazole
Syphilis	Benzathine benzylpenicillin or doxycycline or erythromycin
Bacterial vaginosis	Oral or topical metronidazole or topical clindamycin

Gastrointestinal

Condition	Recommended treatment
Clostridium difficile	First episode: metronidazole Second or subsequent episode of infection: vancomycin
Campylobacter enteritis	Clarithromycin
Salmonella (non-typhoid)	Ciprofloxacin
Shigellosis	Ciprofloxacin

*a combined topical antibiotic and corticosteroid is generally used for mild/moderate cases of otitis externa